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POROKERATOSIS MIBELLI

REPORT OF THREE CASES IN ONE FAMILY; HISTOLOGIC STUDIES

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Mibelli [1] reported the first case of porokeratosis in 1893. Moncorps [2] recorded 95 cases which had appeared in the literature up to 1931. From 1931 to 1941 we have found 24 reports dealing with 37 affected persons.

Geographic location or race does not seem to play an important role. Cases have been observed not only in Italy but in China, Japan, France, Germany, England, Poland, Russia, Argentina, Switzerland and the United States. Lain [3] in 1928 stated that among the 70 cases which he gathered from the literature, including 3 of his own, 20 were from this country. We have found 7 cases reported in the United States in the past decade. The patients whose cases were reported by Ambler and Stout [4] and by Johnson [5] were both Negroes.

CLINICAL AND HISTOLOGIC CHARACTERISTICS

Because of the repeated clinical and histologic descriptions of porokeratosis Mibelli in the literature, we shall confine ourselves to a brief description of the most essential features. Clinically, there are different types of eruptions observed in porokeratosis. The most characteristic

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1. Mibelli, V.: Contributo allo studio della ipercheratosi dei canali sudoriferi (Porokeratosis), Gior. ital. d. mal. ven. **28**:313, 1893; An Uncommon Form of Keratodermia: "Porokeratosis," in Unna, P. G.: International Atlas of Rare Skin Diseases, Leipzig, L. Voss, 1893, vol. 9.

2. Moncorps, C.: Porokeratosis Mibelli, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankeiten, Berlin, Julius Springer, 1931, vol. 8, pt. 2, p. 463.

3. Lain, E. S.: Porokeratosis; Report of Three Cases, Urol. & Cutan. Rev. **32**:383 (June) 1928.

4. Ambler, J. V., and Stout, K. L.: Porokeratosis (Mibelli): Report of Its Occurence in Negro, Arch. Dermat. & Syph. **29**:20 (Jan.) 1934.

5. Johnson, H. H.: Porokeratosis (Mibelli), Arch. Dermat. & Syph. **34**:574 (March) 1941.

and the one usually encountered is the round, oval or irregular gyrate plaque. It is smooth or centrally depressed and is surrounded by a raised keratotic wall. The wall is surmounted by a fine groove, from which horny comblike lamellas may protrude. Another type of lesion is the tiny keratotic wartlike papule, or the annular lesion, several millimeters in diameter, which is surrounded by a raised horny wall with a central horny plug or depression. This small lesion, called by Freund [6] forma minima, has a tendency to coalesce with other similar lesions to form a third variety, characterized by linear streaks and resembling a linear nevus. This tendency is conspicuous and frequently observed. We found it in 1 of our cases and in 6 others reported in the last decade by Ichteiman,[7] Freund,[6] Comel,[8] Sugimoto,[9] Tamponi [10] and Jausion and Lévy-Coblentz.[11] A fourth type of lesion consists of massive horny formations as described in the cases of Verrotti,[12] Santojanni,[13] Kobayasi [14] and Casazza.[15]

The extension of a lesion of porokeratosis is usually centrifugal, slow and insidious in onset, leaving a somewhat atrophic area in the center free of hair and glandular structures. A small lesion may gradually change into a characteristic large plaque, or it may remain unchanged for years or forever. A patch may disappear on rare occasions, leaving a slightly atrophic area or apparently normal skin. This has occurred in 1 of our cases and in the case described by Vigne, Lagarde and Lombard.[16]

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6. Freund, E.: Ungewöhnlicher Fall von systematisierter Porokeratosis Mibelli bei einem Kind (Forma minima), Arch. f. Dermat. u. Syph. **170**:2, 1934.

7. Ichteiman, M. S.: Clinical and Histological Study of Porokeratosis Mibelli, Sovet. vestnik. venerol. i dermat. **9**:674 (Nov.-Dec.) 1931.

8. Comel, M.: Porocheratosi sistematizzata zoniforme in bambina, Boll. Soc. ital. di dermat. e sif. **12**:118 (Aug.) 1934.

9. Sugimoto, T.: Ein Fall von systematisierter sogenannter Porokeratosis (Mibelli), Acta dermat. **29**:131 (June) 1937.

10. Tamponi, M.: Ein ungewöhnlicher Fall von Mibellischer Porokeratosis (Kleinste zonenförmige Art), Arch. f. Dermat. u. Syph. **175**:476, 1937.

11. Jausion, and Lévy-Coblentz: Kératose polymorphe du membre supérieur avec porokératose d'un fuseau digito-palmaire, Bull. Soc. franç. de dermat. et syph. **47**:134 (April) 1940.

12. Verrotti, G.: Un caso singolare della "porocheratosi" di Mibelli con corneomi a gruppo: rilievi di ordine istopatogenetico, Gior. ital. di dermat. e sif. **74**:3 (Feb.) 1933.

13. Santojanni, G.: Un caso di porocheratosi di Mibelli con intenso e raro processo ipercheratosico, Arch. ital. di dermat., sif. **9**:204 (March) 1933.

14. Kobayasi, T.: Generalized Porokeratosis Mibelli with Lesions of the Buccal Mucosa and of the Nails, Jap. J. Dermat. & Urol. **36**:439 (Oct.) 1934.

15. Casazza, R.: Morphologische Untersuchungen eines Falles von Porokeratosis Mibelli mit aussergewöhnlich starken Hornwucherungen, Arch. f. Dermat. u. Syph. **170**:12, 1934.

16. Vigne, P.; Lagarde, M., and Lombard, R.: Trois cas familiaux de porokératose de Mibelli, Marseille-méd. **75**:407 (Oct. 5-15) 1938.

The most conspicuous histologic feature is seen particularly in the plaque type of lesion, which is surrounded by a raised wall and a fine groove. It is the horny plug which emerges from the groove in the form of a horny comb, designated by Mibelli as a cornoid lamella, that signifies atypical incomplete cornification. Indeed, one sees in the otherwise massive horny layer a streak of horny substance which dips into the epidermis and differs from the rest of the horny layer by its color (particularly when stained with special stains, such as safranine or Van Gieson's stain) and by its content of nuclei or nuclear fragments. Occasionally clumplike formations resembling *corps ronds* or grains as observed in Darier's disease have been described (Gilchrist [17] and Ichteiman [7]). The granular layer in this area is absent, and the malpighian layer is thinned, in contrast to the neighboring acanthotic epidermis. Other signs of disturbed function of the epidermal cells in the region of the cornoid lamella are evidenced by the pyknosis or absence of nuclei and in the homogenization and swelling of the epidermal cells.

In a small annular lesion the characteristic cornoid plug is usually absent. Instead, there is a depression in the epidermis filled with horny material containing round or parakeratotic nuclei.

The name of porokeratosis was given to this disease entity by Mibelli because his histologic investigations convinced him that the cornoid lamella originated from the sweat duct. This contention, however, was opposed by Ducrey and Respighi,[18] Matsumoto [19] and other Japanese authors, Ichteiman,[7] Miescher [20] and many others. These authors denied the dependence of the pathologic process on the sweat duct. They found the characteristic histologic lesion developed also in follicles or in other areas free of any glandular structures. They considered the term porokeratosis, therefore, a misnomer.

HEREDITARY ASPECT

Although porokeratosis is definitely of hereditary nature—the mode of inheritance is considered one of regular dominance—many reported cases are solitary and not familial. Thus, among 33 cases taken by Fulde [21] from the literature up to 1923 only 14 were familial, and among

17. Gilchrist, T. C.: A Case of Porokeratosis (Mibelli) or Hyperkeratosis Excentrica (Respighi) with a Remarkable Family History, J. Cutan. Dis. **15**:386 (Aug.) 1897.

18. Ducrey, A., and Respighi, E.: Sur une singulière dermatose à localisations cutaneés et muqueuses: L'hyperkératose figurée centrifuge atrophiante (improprement appelé porokératose); nouvelle étude clinique et histologique, Ann. de dermat. et syph. **9**:609, 1898.

19. Matsumoto, S. I.: The So-Called Porokeratosis, J. Cutan. Dis. **36**:379 (July) 1918.

20. Miescher, G.: Ueber "Porokeratosis Mibelli," Arch. f. Dermat. u. Syph. **181**:532, 1940.

21. Fulde, E.: Studien über Vererbung von Hautkrankheiten: IV. Porokeratosis Mibelli, Arch. f. Dermat. u. Syph. **144**:6, 1923.

the 24 cases reported in the last decade we find only 4 to have been familial. This preponderance of solitary cases is, in our opinion, more apparent than real, for the family history is frequently disregarded, or, if recorded, it is not based on personal and thorough investigation of the other members of the family. In anomalies like porokeratosis personal examination is particularly necessary, as the lesions may be easily overlooked when they are of the small verruca-like variety. The not infrequent appearance of the lesions in adult life may also account for a number of the solitary cases. Negative data in regard to familial occurrence are, therefore, frequently incorrect. This may also explain why in analyzing many cases in the literature one finds the ratio of affected to normal siblings less than 1 : 1, the ratio expected of regular dominance. Cockayne [22] gave another reason for regular dominance, namely, that in none of the familial cases analyzed by him was the anomaly transmitted from one generation to another through a person definitely determined to be free of the disease.

The different types of lesions may be present in different members of the same family or in the same person. While the predisposition to porokeratosis is inherited, the type of lesion is not inherited. Thus, in the family we studied, in addition to the small annular lesion, the father showed the characteristic plaques on the fingers, while one son showed the linear type on his neck. This observation was made also by Fulde.[21]

A striking feature of porokeratosis Mibelli is the partial sex limitation, for it occurs more often in males. Fulde and Cockayne found a ratio of 3 : 1 in favor of males. Among the 37 cases in the literature of the last decade we found 28 males and 9 females affected, a ratio of more than 3 to 1.

We had occasion to see at the New York Skin and Cancer Hospital, service of Dr. I. Rosen, a boy aged 16 with porokeratosis Mibelli. Personal investigation of the members of the family revealed the presence of this anomaly also in the father and in a younger brother. The mother, her daughter and three sons from a previous marriage were free of cutaneous lesions (the latter three could not be examined personally). The father stated that his father had had a similar eruption on the fingers. We were able to make some studies of one of the boys and his father, and we consider our findings of sufficient interest to present them in this report.[23]

REPORT OF CASES

CASE 1.—F. M., a boy aged 16, born of Italian parents, was observed for the first time on Sept. 4, 1941, complaining of an eruption on the neck which had been present since birth.

22. Cockayne, E. A.: Inherited Abnormalities of the Skin and Its Appendages, London, Oxford University Press, 1933, p. 156.

23. These cases were presented by Dr. I. Rosen before the Manhattan Dermatologic Society (Arch. Dermat. & Syph. **45**:782 [April]; 982 [May] 1942).

Examination of the Skin.—On the left side of the neck extending from the lower part of the retroauricular fold downward there was a brownish pigmented band, 3 inches long and ½ inch wide (7.5 by 1.3 cm.), lined by somewhat raised horny borders (fig. 1). The area within the borders appeared depressed and granular. The downward and posterior extension of this linear lesion presented several discrete annular lesions 1 to 3 mm. in diameter showing raised horny borders and hyperpigmented centers. Similar discrete elements were present over the left mastoid area and along the sides of the left cervical linear patch.

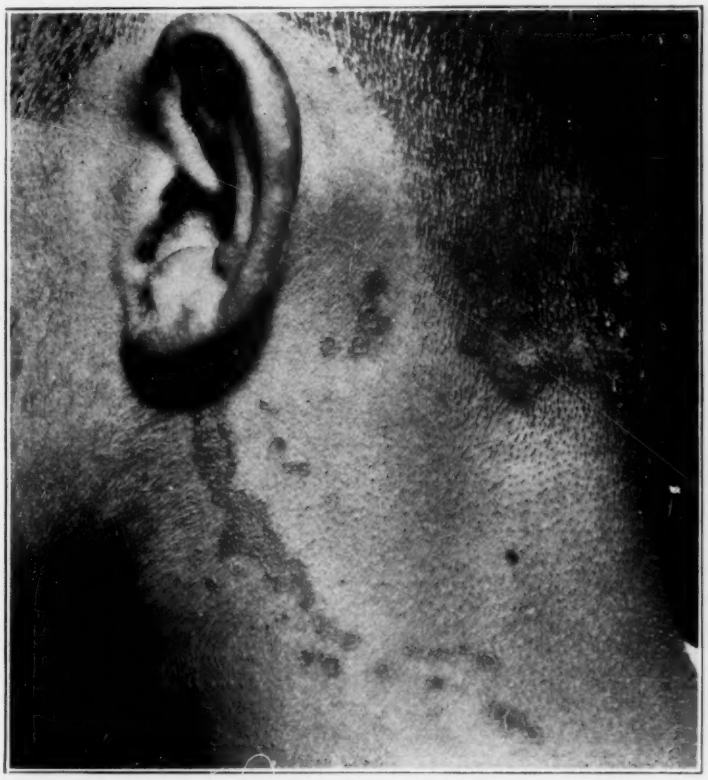

Fig. 1 (case 1).—Patient with porokeratosis Mibelli, showing a brown pigmented band with a horny border and a depressed granular center and also a few outlying discrete annular elements occupying the left cervical area.

A perpendicular patch was present in the center of the nape of the neck. The lower half of this patch showed scarring, the result of electrodesiccation. Several new annular lesions appeared later in the scarred area. The upper end of the linear plaque reached the suboccipital region and ended in a raised crusted verrucous plaque. The crusting was apparently due to pyogenic infection, for it disappeared after application of an antiseptic ointment (fig. 2). On the nose and near the outer canthus of the right eye there were a few tiny annular lesions resembling those on the neck. The dorsal aspect of the base of the left thumb presented a tiny round darkly pigmented papule which resembled a verruca but undoubtedly was a lesion of porokeratosis.

While the linear lesions were said to have been present since birth, no definite information could be elicited from the parents about the duration of the small lesions on the neck and face.

Physical Examination.—General physical examination revealed nothing abnormal.

Laboratory Examination.—The urine was normal, and the Wassermann reaction of the blood was negative. The red and white blood cells were normal in number, appearance and proportion. The clotting time was thirty-seven minutes and the prothrombin time twenty-five seconds. The total carotenoid content of the blood (74 units per hundred cubic centimeters) and the vitamin A content (23 blue units) were normal. The basal metabolic rate was normal (+1 per cent).

Fig. 2 (case 1).—A linear lesion with a raised verrucous plaque at the upper end and a scar at the lower half containing new annular elements.

Histologic Studies (Dr. D. L. Satenstein).—The Linear Lesion on the Left Side of the Neck: The stratum corneum covered the entire section and extended downward into the follicular openings and over a zone overlying the cellular infiltration in the upper part of the cutis (fig. 3). The corneous layer in this area was somewhat densely packed and adherent to the underlying epidermis. The cells contained rounded nuclei that could be mistaken for those seen in parakeratosis. The corneum in the rest of the section was loosely laminated and only slightly adherent to the epidermis. The epidermis in the follicular zone was about three times as thick as in the rest of the section, but in the zone overlying the cellular infiltration it was reduced to a few rows of cells. In the latter area the granular layer was absent, while it was present and irregular in thickness

in the rest of the section. The prickle cells showed considerable hydrops, particularly in the region of the follicles. The basal cell layer was retained in a part of the section only and contained irregularly distributed pigment granules. The epidermis at the edge of the section showed a sweat duct which was dilated and contained horny material (fig. 4). Throughout the cutis there was considerable interstitial edema with some parenchymatous edema in the lower portion of the cutis. The papillary bodies and the rete pegs were somewhat irregular, some being narrowed and others broadened. The blood vessels in the papillary and subpapillary zones were moderately dilated, and there was a sparse cellular infiltration in the perivascular areas. In the area underlying the thin epidermis with the condensed horny layer there was an irregular fairly large focal

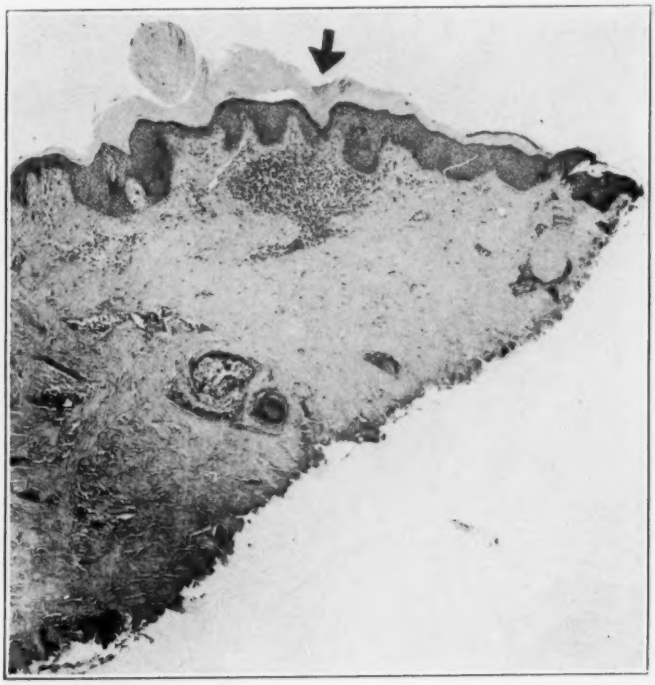

Fig. 3 (case 1).—Photomicrograph of an area of the linear lesion (fig. 2), showing on the right the corneous layer densely packed over a zone of cellular infiltration in the upper part of the cutis (× 40).

infiltration consisting of round cells and occasional swollen connective tissue cells, which were embedded in a fine reticulum containing a few small blood vessels. The cutis in the subepidermic region was granular in some areas. There was irregular grouping of pigment granules, both intracellular and extracellular. The cutaneous appendages were barely noticeable.

A Discrete Small Lesion on the Neck: Tissue removed from an annular lesion on the neck showed histologic features similar to those of the linear lesion. The horny layer was somewhat irregular and in places formed a loosely laminated network. At the follicular openings it appeared somewhat condensed and moderately parakeratotic. The epidermis was somewhat irregular, in some parts thinned and in others thickened. It was particularly thin in one area where the horny

layer was condensed. There was no indication of an underlying follicle in this area. The granular layer was fairly well retained. The cells of the malpighian layer showed considerable hydrops. This was most pronounced in the upper layers but was not of uniform distribution. The palisade layer was well retained and contained in some areas a considerable amount of fine pigment granules. In the cutis the papillary bodies were considerably edematous, particularly in the region of the dilated follicle, and contained dilated vessels with a few round cells and chromatophores. Chromatophores were also present independent of the infil-

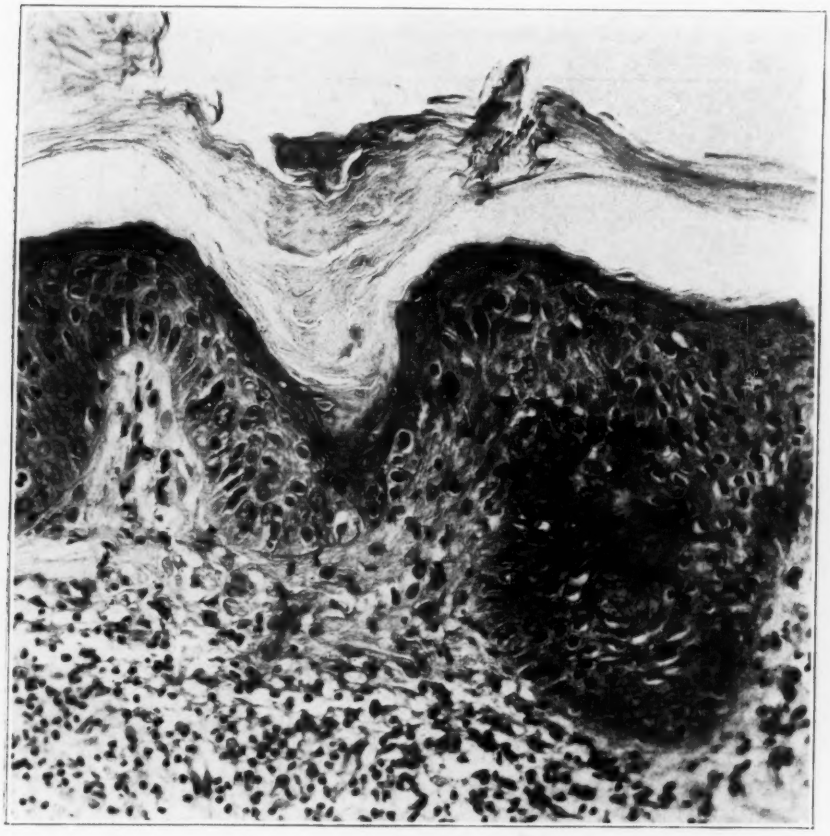

Fig. 4 (case 1).—Photomicrograph of an area at the right in figure 3 (× 290). The densely packed stratum corneum contains rounded nuclei and dips into the follicle. The epidermis over the cellular infiltration is thinner. A dilated sweat duct containing horny material is seen in the rete peg at the right edge of the section.

tration. There was a fairly large cellular infiltration extending down to the midcutis. It was embedded in a fine reticulum containing some capillaries. The infiltrating cells were predominantly small round cells, but there were also a few swollen connective tissue cells.

Summary of Histologic Observations: The essential histologic features seen in the tiny annular lesion and in the linear lesion were similar. The stratum

corneum extended downward in the region of follicular openings, as well as in areas which showed no indication of any follicle or sweat duct. The downward extension consisted of a densely packed corneous layer which contained rounded nuclei, some not due to parakeratosis and others definitely parakeratotic. In an area above a large focal infiltration of the cutis the epidermis was thin and covered by a condensed parakeratotic horny layer. The cells of the prickle layer showed considerable hydrops in the region of the follicle and in the area overlying the dermal infiltration.

Case 2.—J. M., aged 48, the father of F. M. (case 1), a gardener, born in Italy, had an eruption on his fingers which had been present since infancy and

Fig. 5 (case 2).—Ring and gyrate lesions on the left thumb, index and ring finger.

lesions on his face of which he was unaware. The eruption on his fingers did not interfere with his occupation or inconvenience him in any way. Another son, aged 10 (case 3), was also affected. The patient's father is said to have had a similar eruption on his fingers.

Dermatologic Examination.—The eruption consisted of roundish, oval or gyrate plaques about 2.5 cm. in diameter. Each lesion was partly hyperkeratotic, partly smooth, somewhat depressed and surrounded by a raised horny border in which there was a fine blackish discolored groove. In some of the lesions the groove was partly situated within the thickened portion of the plaque, away from the border. There were three such lesions on the fingers of the left hand, namely, on the dorsoulnar aspect of the first phalanx of the thumb and

on the radial aspect of the second phalanx of the index finger and of the middle finger (fig. 5). On the right hand one lesion was situated on the ulnar aspect of the first phalanx of the thumb and another on the radial aspect of the index finger. Below the former lesion there was another, oval and 1.5 cm. in the longest diameter. On the face there were several lentil-sized annular hyperpigmented lesions surrounded by a hypkeratotic border. The patient stated that one large lesion on one of his fingers, resembling the present lesions, disappeared spontaneously without leaving any trace.

Histologic Study of a Plaque on the Left Hand.—With low power magnification considerable acanthosis could be seen. The rete pegs were partly narrowed

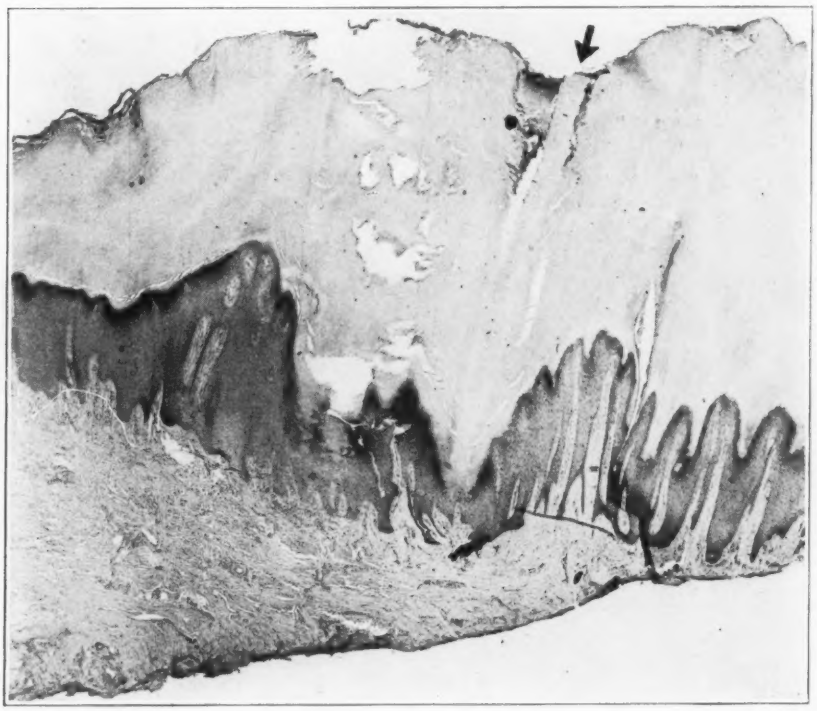

Fig. 6 (case 2).—Photomicrograph of tissue from one of the plaques on the left hand, showing marginated acanthosis with a massive horny layer and the cornoid streak or lamella distinct from the surrounding corneous layer (× 25).

and partly broadened and extended down to the midcutis, while the papillary bodies were altered to fit in between the changed rete pegs. In the central portion of the section there was more or less marginated acanthosis about an area which was comparatively thin. The surface of the epidermis was irregular and covered by a massive horny layer which was adherent to the surface epidermis (fig. 6). In the region where the epidermis was thin there was a streak of horny material distinct from the surrounding stratum corneum (cornoid lamella), which extended from the surface down to the epidermis. With higher magnification it was seen to contain throughout its length considerable debris,

consisting of nuclear remains, while the rest of the horny layer was free of any extraneous substances (fig. 7). Near one edge of another section there was a dilated sweat pore which was filled with horny material. No other part of the sweat apparatus was visible except that located in the epidermis (fig. 8).

The cutis was considerably sclerotic with elongated narrow papillary bodies containing dilated vessels. Cellular infiltration was slight. Numerous fairly

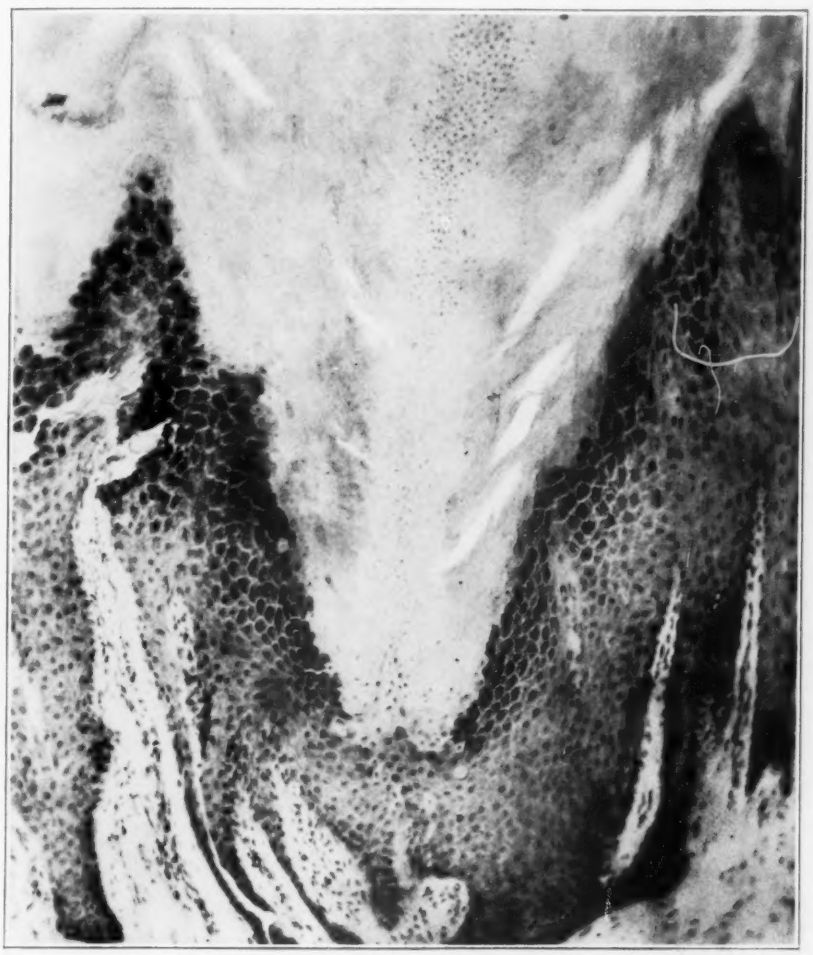

Fig. 7 (case 2).—Photomicrograph of an area in figure 6 (× 115), showing the cornoid lamella containing remains of nuclear debris.

large blood vessels were seen within the subpapillary zone with a spare small round cell infiltration (fig. 6). With high power magnification (not illustrated) a number of fibroblasts were seen throughout the cutis. No sebaceous or sweat glands or hair follicles were observed.

Microscopic studies of numerous specimens of this lesion showed in addition the following changes, which were practically the same in all: The outstanding

feature was the acanthosis, with dense packing of the cells so that the intercellular spaces with the prickle cell bridges were made out with difficulty. Keratohyalin granules were present not only in the cells of the increased granular layer but also scattered throughout the upper part of the epidermis. The horny streak which extended downward to cause thinning of the epidermis contained fine shiny dots (fat droplets) and a considerable number of nuclear fragments.

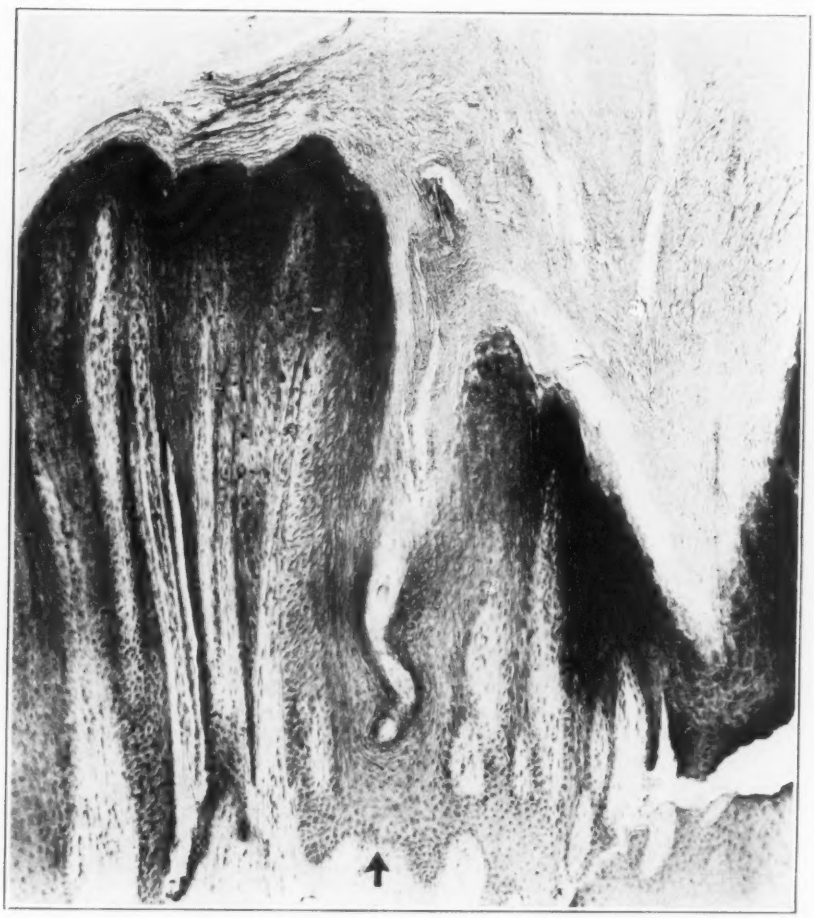

Fig. 8 (case 2).—A dilated sweat pore filled with horny material (× 100).

These fragments extended upward almost to the surface of the horny layer. No distinct parakeratosis could be seen. The dilated sweat pore (fig. 8) was filled with homogeneous horny material. At the mouth of the sweat pore the horny material was somewhat fragmented into clumps which contained keratohyalin granules. In some parts of the section the palisade layer was not distinct. The infiltration in the cutis was of the small cell variety. Some of the vessels were considerably thickened.

In Summary.—The essential histologic features seen in one of the plaques were: (1) considerable acanthosis and hyperkeratosis; (2) a characteristic

so-called cornoid lamella, which consisted of a column of hornlike substance containing nuclear fragments and fat droplets and arising from a thin epidermis deprived of a granular layer; (3) a dilated sweat duct, which had no relation to the cornoid lamella and was filled with horny substance and at the mouth of which the horny layer was fragmented into clumps containing keratohyalin granules, and (4) a sclerotic cutis.

CASE 3.—S. M., a boy aged 10 years, the brother of F. M. (case 1), was found to have a brownish hyperpigmented annular lesion 3 mm. in diameter with a raised horny border, situated in the right cubital fossa. This lesion was said to have been present since infancy.

COMMENT

The presence of linear lesions in one son (case 1), of the characteristic gyrate plaques in the father (case 2) and of the annular form only in another son (case 3) confirms the observation of Fulde and others that the type of lesion may differ in the various members of the family who are predisposed to the disease. The histologic observations in our cases confirm again the contention of those investigators who maintain, contrary to the belief of Mibelli, Hall [24] and others, that the sweat ducts do not play an important role in the pathogenesis of porokeratosis. The one sweat duct observed in the section of the tiny annular lesion and in that of the large plaque showed no relation to the parakeratotic horny plug or to the cornoid lamella, which is considered the most important pathologic feature of the anomaly. The plugs in the tiny annular lesions, which correspond to the cornoid lamella in the more advanced plaque type, indicate by their presence in follicular as well as in nonfollicular areas that, while ducts and follicular ostiums are favored as starting points in the keratotic processes, these structures are not of absolute pathogenetic importance.

The large inflammatory focus of round cells which was present in the tiny annular and in the linear lesion underlying the horny plug has been frequently observed and was the reason for the conception of some authors, such as Verrotti [12] and Ritchie and Becker,[25] that porokeratosis is an inflammatory process. This has been denied, however, by Mibelli,[1] Gans,[26] Hall [24] and others, who called attention to the absence of such inflammatory signs in many early lesions and in most advanced large lesions. They also called attention to the presence of such infiltrations in other keratoses, ichthyosis for instance, which were not considered inflammatory.

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24. Hall, G. A. M.: Porokeratosis (Mibelli): A Report of Its Occurrence in Six Chinese Patients, Arch. Dermat. & Syph. **18**:396 (Sept.) 1928.

25. Ritchie, E. B., and Becker, S. W.: Porokeratosis (Mibelli): Report of a Case; Histologic Study and Animal Inoculation, Arch. Dermat. & Syph. **26**:1032 (Dec.) 1932.

26. Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, p. 83.

We interpret our histologic observations as those due to an abnormal functioning of the epidermal cells, manifested by disturbance in the cornification cycle and by acanthosis, hyperkeratosis, parakeratotic plugs and particularly by the so-called cornoid lamella. Whether the enormous amount of hyperkeratosis and acanthosis seen in the plaque lesion is of secondary nature, as Miescher and others maintain, cannot be definitely decided. We feel that these features are an essential part of the pathologic process. In favor of this contention speaks the not infrequent occurrence of the massive verrucous and corneous type of lesion seen in porokeratosis.

The disease may therefore be considered as a keratodyskeratotic abnormality, the underlying cause of which is to be found in an abnormal germ plasm transmitted from parents to their offspring. This consideration excludes the necessity of calling the lesion a nevus, in spite of the strong tendency of porokeratotic lesions to arrange themselves in linear and systematized configuration. We consider it a traditional mistaken conception to consider all linear and unilaterally arranged lesions as nevi. We know that dermatoses of definitely inflammatory nature, like herpes zoster, eczema, lichen planus and psoriasis, may have a linear and unilateral distribution and are nevertheless not nevi. Darier's disease, which is designated not as a nevus but as an inherited dyskeratotic anomaly, has a similar tendency to linear formation. We explain the tendency of porokeratosis to linear configuration by stating that the same morbid factor which induces the lesion to extend centrifugally—which is one of the most characteristic features of the anomaly—is also responsible for the linear extension of the lesions, observed in many cases.

The knowledge that the underlying cause of this cutaneous abnormality is a faulty gene does not eliminate the necessity of looking for or the hope of finding facts which may further elucidate the pathogenic mechanism of this disease. The thought that the dysfunction of the epidermal cells may be based on an abnormal physiologic-chemical nature of the cells themselves or on a faulty or deficient supply of substances from the general system must lead to investigations in these two directions. In analogy with Darier's disease, it might be possible to find a derangement in vitamin A metabolism, as Peck [27] has found in Darier's disease. Indeed, Vigne, Lagarde and Lombard [16] seem to have had this thought, for they reported a diminished vitamin A content in the blood of 1 of their patients. We, however, could not substantiate this finding in any of our cases. A diminished basal metabolic rate was found by Ambler and Stout [4] in their case, but thyroid therapy was unsuccessful.

27. Peck, S. M.; Chargin, L., and Sobotka, H.: Keratosis Follicularis (Darier's Disease), Arch. Dermat. & Syph. **43**:223 (Feb.) 1941.

Acton,[28] however, reported a complete cure in 3 cases of porokeratosis Mibelli by this treatment. An abnormal basal metabolic rate was not found in one of our patients who was thoroughly investigated.

SUMMARY AND CONCLUSIONS

A family is described in which three members, a father and his two young sons, were affected with porokeratosis Mibelli. The grandfather of these boys was said to have had similar lesions. One member showed only the tiny annular form, while the two others had in addition the linear and gyrate plaque lesions respectively.

Histologic studies of the different lesions confirm the opinion shared by many investigators that the sweat duct is not essential for the pathologic process of porokeratosis. We therefore consider the term porokeratosis a misnomer.

The anomaly is a hereditary keratodyskeratosis. Further elucidation of the pathogenetic mechanism is to be expected from progress in the knowledge of the physiologic-chemical nature of the cells or from studies of the various general metabolic and chemical processes of the affected members of these families. In these studies one should seek also the explanation for the partial sex limitation of this disease.

135 East Fiftieth Street.

853 Seventh Avenue.

28. Acton, H. W.: Porokeratosis: Its Causation and Treatment, Indian J. M. Research **15**:349 (Oct.) 1927.

STUDIES ON OINTMENTS

II. OINTMENTS CONTAINING SALICYLIC ACID

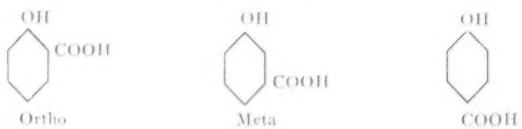
ERNEST A. STRAKOSCH, M.D.

MINNEAPOLIS

The first part [1] of my studies on ointments dealt with the penetration of fifteen bases into the intact human skin. The present report is a continuation of these studies.

Salicylic acid was synthetically produced from phenol in the year 1860 by Kolbe and Lautermann,[2] and Kolbe devised a commercially practical synthetic process in 1874.

Salicylic acid is an orthooxybenzoic acid.



Only the orthobenzoic acid has pharmacologic action; the metabenzoic and parabenzoic acids are pharmacologically inactive.

The solubility of salicylic acid is, according to Moncorps,[3] as follows: One part of salicylic acid dissolves in 13 parts of boiling water, in 444 parts of water at a temperature of 15 C., in 500 parts of water at 20 C., in 60 parts of glycerin, in 45 parts of olive oil and in 7 parts of castor oil.

The antiseptic action of salicylic acid is about equivalent to that of phenol. A salicylic acid solution of 1:1,000 has the same antiseptic action as a phenol solution of 1:850.

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The second condensed part of a thesis submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Dermatology and Syphilology.

1. Strakosch, E. A.: Studies on Ointments: I. Penetration of Various Ointment Bases, Dermatologica, to be published.

2. Cited by Sollmann, T.: A Manual of Pharmacology, Philadelphia, W. B. Saunders Company, 1932, p. 621.

3. Moncorps, C.: Untersuchungen über die Pharmakologie und Pharmakodynamik von Salben und salbeninkorporierten Medikamenten: Ueber die Resorption und Pharmakodynamik der salbenincorporierten Salizylsäure, Arch. f. exper. Path. u. Pharmakol. **141**:50, 1929.

The action of salicylic acid is diminished in the presence of alkali, which binds acid. The alkaline salt sodium salicylate is considered less effective than the free acid.

Salicylic acid is a drug which is most often applied in ointment form, as its action is utilized in three ways in dermatology: (1) to produce a keratolytic or macerating action; (2) as an antiseptic (and it has some antiparasitic action), and (3) on the assumption that its addition to an ointment will beneficially influence the absorption of the other incorporated drugs.

Its absorption through the skin was established by Aubert,[4] DuMesnil,[5] Linossier[6] and many others.[7]

Sokolov,[8] while working on the absorption through the skin of potassium iodide, bromide and chloride from petrolatum or hydrous wool fat, concluded that all these salts were absorbed only when salicylic acid was added to the ointments. He believed that the keratolytic action of salicylic acid was absolutely necessary for the absorption of any drug, that it acted as a kind of "path maker," a theory which was disputed by Gundorow[7d] a few years later. Sokolov, however, was partly right. Rojahn and Wirth[7g] showed, for example, that esters of salicylic acid were much better absorbed when free salicylic acid was present. There is, however, some experimental evidence that the addition of salicylic acid to certain chemicals, for example to tars, will

4. Aubert, P.: Expériences sur l'absorption cutanée, Ann. de dermat. et syph. **3**:1037, 1892; Le corps gras et l'absorption cutannée, Lyon méd. **75**:524, 1894.

5. DuMesnil, T.: Ueber das Resorptionsvermögen der menschlichen Haut, Deutsches Arch. f. klin. Med. **50**:101, 1892.

6. Linossier, M. G.: Absorption par la peau de l'acide salicylique, Lyon méd. **3**:84, 1894.

7. (*a*) Linossier, M. G., and Lannois, M.: De l'absorption de l'acide salicylique par la peau, Lyon méd. **25**:250, 1895. (*b*) Schwenkenbecher: Das Absorptionsvermögen der Haut, Arch. f. Physiol. **1**:121, 1904; Ueber die Ausscheidung des Wassers durch die Haut von Gesunden und Kranken, Deutsches Arch. f. klin. Med. **79**:29, 1903-1904. (*c*) Filehne, W.: Ueber die Durchgängigkeit der menschlichen Haut für flüssige und feste Stoffe, Berl. klin. Wchnschr. **35**:45, 1898. (*d*) Gundorow, M.: Das Resorptionsvermögen der intakten Haut, Arch. f. Dermat. u. Syph. **71**:17, 1904. (*e*) Moncorps.[3] (*f*) Leslie-Roberts, H.: On the Absorption of Salicylic Acid by the Human Skin, Brit. J. Dermat. **40**:325, 1928. (*g*) Rojahn, C. A., and Wirth, E.: Ueber den Grad der perkutanen Resorption der Salicylsäure sowie ihrer Salze and Ester aus Rheumamitteln des Handels, Arch. f. exper. Path. u. Pharmakol. **175**:26, 1934. (*h*) Brown, E. W., and Scott, W. O.: The Absorption of Methyl Salicylate by the Human Skin, J. Pharmacol. & Exper. Therap. **50**:32, 1934.

8. Sokolov, N. M.: Ueber die Resorption einiger Salze durch die Haut bei Einreibung derselben in Form von Salben, Arch. f. Dermat. u. Syph. **30**:115, 1895; **35**:271, 1896.

cause severe irritation (Siemens [9]). The effect of the addition of salicylic acid to different drugs, such as sulfur and various tars, will be discussed in further publications.

If salicylic acid is allowed to act on the skin, it will cause a whitish discoloration. Hodara [10] showed, however, that an alcoholic solution of it without air-tight dressing is without effect. There was no peeling. The same observation was made with an aqueous solution. He even went so far as to state that a keratolytic action of salicylic acid, regardless of its vehicle (a fat, alcohol or water), can be expected only if a dressing is applied on top of the application. He showed on microscopic sections that salicylic acid causes a colliquation in the rete Malpighii, which eventually leads to a separation of the epidermis from the basal layer, while the basal cells as such remain intact; but he concluded that this will happen only when the drug in some vehicle is covered by a bandage. It was Menschel [11] who showed that the action of salicylic acid is rather a retecytolysis than a colliquation, that it comes to an edema formation in the rete Malpighii, but without its local destruction, and that a new stratum corneum is quickly formed under the irritating and stimulating effect of the acid. But, he pointed out, this effect is not specific for the salicylic acid and can also be produced with potassium hydroxide even in a concentration as low as 1 : 5,000. The point of action according to this author is the horn albuminoids. If by means of an air-tight bandage the perspiratio insensibilis is suppressed, then, Menschel argued, there is a swelling of the horn albuminoids, which in turn will facilitate the action of the salicylic acid and so increase its action.

Whether one is willing to accept this theory or not, it is a well known fact that a bandage tightly applied on the skin—and it does not even have to be air tight—will cause stagnation of the sweat secretion and therefore some maceration of the skin. It stands to reason that any drug will be better absorbed through a macerated epidermis than through a normal one. This is the principle, for instance, of the use of salicylic acid plasters. Menschel confirmed Hodara's work. He, too, thought that an air-tight bandage over the application was essential for the keratolysis, although he was not quite sure whether keratolysis to some extent could not be produced by means of salicylic acid containing ointments without a bandage.

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9. Siemens, H. W.: Die experimentell-therapeutische Analyse der Dreuwschen Salbe, Arch. f. Dermat. u. Syph. **179**:580, 1939.

10. Hodara, M.: Histologische Untersuchungen über die Einwirkung der Salicylsäure auf die gesunde Haut, Monatsh. f. prakt. Dermat. **23**:117, 1896.

11. Menschel, H.: Zur Kolloidchemie und Pharmakologie der Keratinsubstanzen der menschlichen Haut, Arch. f. exper. Path. u. Pharmakol. **110**:1, 1925.

Moncorps,[12] in the course of an extensive investigation, was the first one to examine the absorption of salicylic acid from different ointment bases by measuring the urinary excretion of the drug. He also tried to determine the beginning of keratolysis caused by salicylic acid from the different bases. He, too, used the air-tight bandage method.

By determining the urinary excretion of salicylic acid from different ointment bases, Moncorps found (using always the same concentration of 5 per cent) an increasing absorption of salicylic acid from lard over a zinc paste, yellow petrolatum, hydrous wool fat, a mucilage without fat,[13] a mucilage with 30 per cent fat,[13] an oxycholesterol-petrolatum base [14] and a mucilage with 30 per cent fat,[13] an oxycholesterol-petrolatum base [14] and a mucilage with 50 per cent fat.[13] The excreted amount of salicylic acid was in a proportion of 1 : 1.2 : 2.4 : 3 : 8.4 : 10 : 15 : 40; in other words, the minimum absorption was from lard, amounting to 0.29 per cent, and the maximum from the mucilage with 50 per cent fat (an oil in water emulsion), amounting to 11.82 per cent of the applied amount of salicylic acid after twenty-four hours.

The same keratolytic effect was noted from 0.5 to 1 per cent of salicylic acid in the oxycholesterol-petrolatum base or in the mucilage with 50 per cent fat or from 5 per cent salicylic acid in hydrous wool fat or petrolatum and from a 15 per cent concentration in zinc paste or lard.

EXPERIMENTAL STUDIES

Experiments were carried out with salicylic acid in different concentrations in various bases to determine first the necessary concentration in various bases which will produce keratolysis on the normal human skin and also the time which is necessary for its production.

It was first attempted to test the ability of the various bases to give up the incorporated salicylic acid into another medium. I was fully aware that the results of this experiment did not correspond with the actual clinical happenings on the skin. All that it should demonstrate is that there is a difference among various bases in liberating an incorporated drug.

Six ointments containing 1 per cent salicylic acid were made with the following bases: (1) petrolatum; (2) petrolatum and hydrous wool

12. Moncorps, C.: Untersuchungen über die Pharmakologie und Pharmakodynamik von Salben und salbeninkorporierten Medikamenten, Arch. f. exper. Path. u. Pharmakol. **141**:50 and 87, 1929.

13. The mucilage without fat was called physiol A; the mucilage plus 30 per cent fat, physiol B, and the mucilage plus 50 per cent fat, physiol C. The kind of fat was not named. For further reference see Zakarias, L.: Ueber stabile Polysaccharide als Grundlagen für therapeutische und kosmetische Salben, Chemiker-Ztg. **51**:321, 1927; Mod. Parfümerie **20**:114, 1927.

14. The oxycholesterol-petrolatum ointment base was eucerin, the German equivalent of the base used in the present studies (aquaphor).

fat in equal parts (water in oil emulsion); (3) a base consisting of 6 per cent of a group of esters of cholesterol (chiefly oxycholesterol) in an aliphatic hydrocarbon (petrolatum) base[15]; (4) a base containing fatty acid esters of diethanolamine mixed with petrolatum,[16] and two bases whose formulas follow:

(5)	Stearyl alcohol[16a]	10.0 Gm.
	Liquid petrolatum	10.0 cc.
	Water	10.0 cc.
	Petrolatum, light	70.0 Gm.
(6)	Zinc oxide	7.5 Gm.
	Talc	7.5 Gm.
	Petrolatum, to make	30.0 Gm.

Bases 2, 3 and 4 are water in oil emulsions, while base 5 is an oil in water emulsion.

Liberation of Salicylic Acid, as Judged by Discoloration of Iron Chloride Solution

Base *	Color of Iron Chloride Solution	
	24 C.	37 C.
Petrolatum	Faint bluish hue	Slight violet
Petrolatum-hydrous wool fat	Slightly violet	Pale violet
Oxycholesterol-petrolatum	Dark violet	Deep, dark violet
Fatty acid esters of diethanolamine	Dark violet	Deep, dark violet
Stearyl alcohol	Dark violet	Dark violet
Zinc oxide	Unchanged	Bluish

* In most instances only the active or most important ingredient of the base is specified here, since a complete description appears in the text.

Five-tenths gram of each ointment was pressed between two strips of filter paper and immersed in little beakers containing equal amounts of a 1 per cent solution of iron chloride. The liberation of the salicylic acid was judged from the degree of violet discoloration of the solution. The results after twelve hours at room temperature (24 C.) and at a temperature of 37 C., to simulate more closely the condition of the skin, are seen in the accompanying table. The second experiment indicated that the liberation of the drug increases with the elevation of the temperature.

15. The preparation was aquaphor, manufactured by the Duke Laboratories Inc., Stamford, Conn.

16. The preparation used was hydrosorb, manufactured by the Abbott Laboratories, North Chicago, Ill.

16a. The preparation used was lanette wax SX, supplied by R. F. Revson Company, New York.

Salicylic acid was next incorporated in the strength of 1, 3, 5, 10 and 15 per cent in the aforementioned six bases.

Only normal persons were used for the investigation. The subject was given a bath before the first application, but no further preparation, such as clipping the hairs, shaving the skin or washing with alcohol, was used. Five-tenths gram of each ointment was slightly rubbed into areas 2 by 2 inches (5 by 5 cm.) in size by means of a glass spatula.

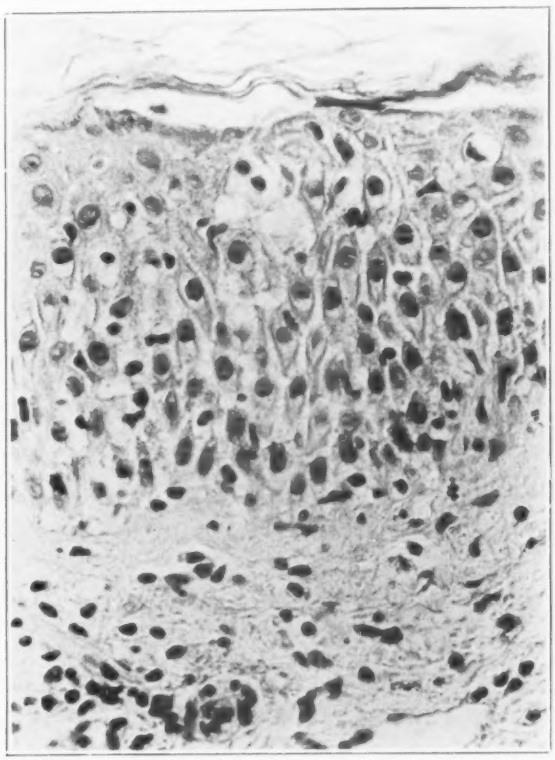

Fig. 1.—Section showing the effect of 5 per cent salicylic acid in petrolatum and hydrous wool fat (equal parts) after ten days. Note the exfoliation of the stratum corneum and the severe intracellular and intercellular edema.

The applications were made on the anterior aspects of the upper parts of the thighs and sometimes on the abdomen. No bandage was applied, and precautions were taken to prevent the wiping off of the ointment as much as possible. In order to simulate practical conditions, the applications were made three times daily. Specimens for biopsy were taken with a punch after block anesthesia with a 1 per cent solution of procaine hydrochloride after twenty-four, forty-eight and seventy-two hours and

after seven, ten and in some cases fourteen days. Each experimental series was made on the same subject, and each series was repeated four times on different subjects. Every subsequent reported result is the average of these four experiments.

The histologic changes in the skin after the application of salicylic acid were described by Gans [17] as follows:

The salicylic acid after application for several days causes a swelling and exfoliation of the stratum corneum. The lamellas become thicker with stronger

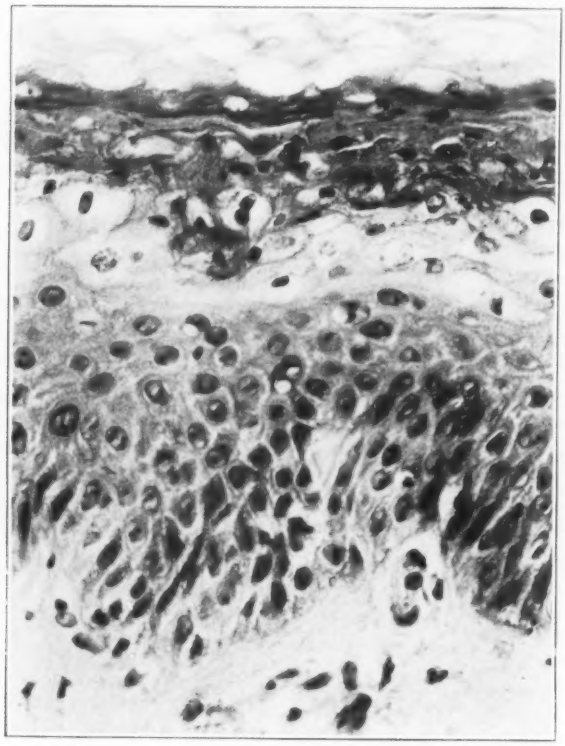

Fig. 2.—Section showing the effect of 10 per cent salicylic acid in an ointment base containing fatty acid esters of diethanolamine after forty-eight hours. Note the swelling of the stratum corneum, the superficial necrosis and the intracellular and intercellular edema.

concentration of the salicylic acid. With prolonged action of the drug, the stratum spinosum and stratum granulosum become broader owing to the intercellular edema, which at first is minimal but increases and finally results in homogeni-

17. Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, p. 217.

zation and necrosis. This change is not uniform but generally occurs faster with stronger concentration of salicylic acid. A new formation of cells begins in the deeper layer, which leads to a considerable acanthosis and to formation of a broad stratum granulosum and stratum corneum, which eventually lift up the necrotic masses in the form of scales. There is merely a slight inflammation in the cutis, in the form of vascular dilatation and proliferation of the perithelium. The chromatin of the nuclei of the connective tissue cells becomes drawn out to long and irregular forms and finally breaks up into small parts (chromatorhexis). There is no leukocytic infiltration.

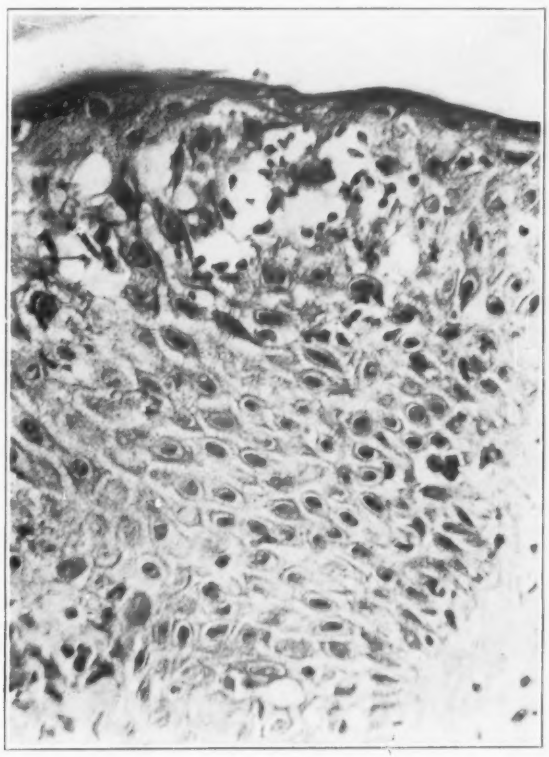

Fig. 3.—Section showing the effect of 10 per cent salicylic acid in petrolatum and hydrous wool fat (equal parts) after ten days. Note the beginning of the vesicle formation.

Depending on the severity of the reaction, however, one finds many lymphocytes and eosinophils in the tissue of the cutis and papillary body.

The relation of the concentration of salicylic acid in various bases to the onset of the keratolytic effect is shown in figure 5.

COMMENT

The conclusion from Moncorps's findings is that the keratolytic effect of salicylic acid runs parallel with the absorption of the drug from

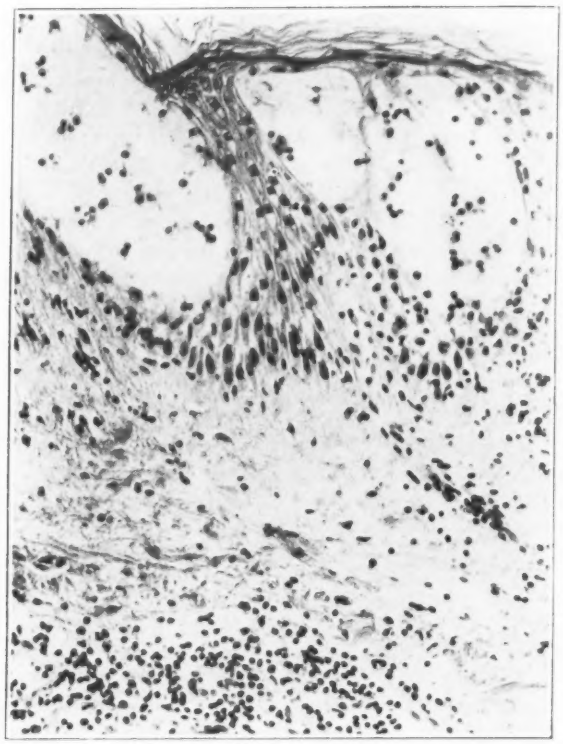

Fig. 4.—Section showing the effect of 10 per cent salicylic acid in an ointment base containing fatty acid esters of diethanolamine after seven days. Note the vesicle formation and the round cell infiltration and vascular dilatation in the corium.

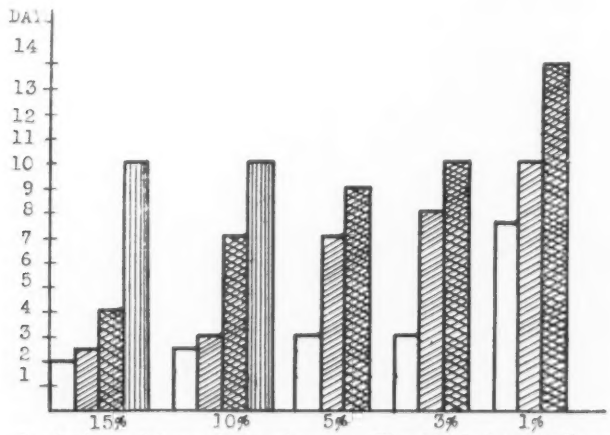

Fig. 5.—Beginning of keratolytic changes. The blank bars indicate the oxycholesterol-petrolatum base, the base containing fatty acid esters of diethanolamine and the one containing stearyl alcohol; the bars with diagonal lines, the petrolatum and hydrous wool fat mixture; the bars with diagonal crisscross lines, petrolatum; the bars with vertical lines, zinc oxide paste.

the various bases. I have not attempted to repeat all his absorption experiments, for I was not as much interested in the speed and amount of absorption as in its local action. However, in the few instances in which the urinary excretion of salicylic acid was determined, my results were almost identical with those of Moncorps. The method used was a modification of Sauerland's technic.[18]

Although the speed and amount of the absorption of salicylic acid from the different bases may be of only theoretic interest, the practical implication of it has to be considered, for the drug in question is not indifferent and causes occasional allergic reactions. A fatal incident was reported by Sannicandro.[19]

My findings on the keratolytic effects of salicylic acid in different concentrations from different bases differ considerably from Moncorps's results. This may be due to the different technic used. He worked with bandage over the ointments, while I did not. But even in the few cases in which I used his technic I was not able to produce keratolysis after a time as short as he reported.

Two points in figure 5 are striking and of special interest. The first is concerned with the manner in which the rate of absorption is influenced by the concentration of salicylic acid. One per cent salicylic acid in a mixture of petrolatum and hydrous wool fat, for instance, caused keratolysis at ten days, while with a 3 per cent concentration in the same base it took about eight days to obtain the same result. With the other bases there was a similar relation between concentration and keratolytic effect. When the concentration was increased from 3 to 5 per cent, equal keratolytic actions were obtained in a shorter period. When the concentration was increased from 5 to 10 per cent, the time to produce keratolysis was reduced not to half but to approximately a third.

Thus there is a direct relation between concentration of the salicylic acid and the time necessary to produce the same keratolytic action. Doubling the concentration shortens the time but does not reduce it to half.

The second interesting point is that increasing the concentration above 10 per cent causes little difference in keratolytic effect. A 10 and a 15 per cent concentration gave, for practical purposes, identical results. In carrying it further, some experiments were made with a

18. Sauerland, F.: Ueber die Resorption von Arzneimitteln aus Salben bei Anwendung verschiedener Salbengrundlagen, Biochem. Ztschr. **40**:56, 1912.

19. Sannicandro, G.: Morte inopinata da applicazione di pomata salicilica (studio clinico ed anatomo-patologico e contributo alla conoscenza della cosidetta "acidosi salicilica"), Dermosifilografo **12**:273, 1937.

20 per cent concentration, and here again the differences in the degree of keratolysis and the time necessary to produce it were almost negligible.

Although there is a decided difference in the effect of salicylic acid from different bases, I was unable to confirm the results obtained by Moncorps, who stated that the best effect was found when an oil in water emulsion was used as a base.

I am aware that all these results and the conclusions one may draw from them cannot be directly applied to the diseased skin, in which the conditions are much more complicated. The amount and the degree of the inflammation in the skin, maceration of the epidermis, elevation of temperature and many other factors will influence the action of the locally applied drug. As it is practically impossible in pathologic conditions to find a base line for comparison, similar experiments on diseased skin would be futile.

SUMMARY

1. The literature on the absorption of salicylic acid through the skin and the local action of it has been reviewed.

2. Salicylic acid was incorporated in the strength of 1, 3, 5, 10 and 15 per cent in the following bases: (1) petrolatum; (2) equal parts of petrolatum and hydrous wool fat; (3) an oxycholesterol-petrolatum ointment base; (4) fatty acid esters of diethanolamine in petrolatum; (5) stearyl alcohol in liquid petrolatum, water and petrolatum, and (6) zinc oxide in talc and petrolatum. The keratolytic action of these ointments on normal human skin was studied histologically. Biopsies were performed after one, two, three, seven, ten and fourteen days.

3. The relation of the different concentrations of salicylic acid in the aforementioned bases to the onset of the keratolytic effect was studied. It was found that there is a direct relation between the concentration of the drug and the time necessary to produce the same keratolytic action. Doubling the concentration shortens the time but does not reduce it to half.

4. Under the experimental conditions described, it was found that salicylic acid produces a keratolytic effect in a shorter time when it is employed in an emulsion base than when it is incorporated in petrolatum or in a zinc paste.

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CONCURRENT, COMBINED AND CONSECUTIVE FUNGOUS INFECTIONS OF THE SKIN

CULTURAL EXPERIENCES

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In a prior communication [1] we have stressed the close relation which usually exists between the clinical appearance of a superficial fungous eruption and the species of infecting micro-organism responsible for it. Increased experience tends to corroborate this phase of practical mycology. We have found that repeated cultures have often resulted in finding of a suspected fungus when the first attempt was barren of results or productive of only nonpathogenic strains of fungi.

Determinative procedures available for investigating suspected fungous infections of the skin are sometimes inadequate to enable one to decide whether the fungus found on culture is primarily causative or a secondary invader. The mere finding of certain fungi which are of known pathogenic titer is usually considered sufficient evidence of pathogenicity. However, one may be in error if one trusts one's ability to obtain pathogenic material in any given case unless there is opportunity for prolonged study and a number of chances to obtain cultural material under different conditions. While it is frequently stated that only when treatment has not been given is the subject optimal for cultural investigation, we believe that treatment for a short period may enhance the prospect of recovering a pathogenic fungus, since the air-borne and other contaminants are thereby eliminated. Saprophytic fungi and bacteria present in the specimen planted in a culture medium may prevent the growth of a pathogenic fungus, and thus a mistaken impression may be obtained.

During the calendar years of 1940 and 1941 we have examined in the mycologic laboratory 1,200 patients suspected of having a fungous disease. Many of the patients were referred with an irrelevant diagnosis

Aided by a grant from the John and Mary R. Markle Foundation.

From the New York Hospital and the Department of Medicine (Dermatology) Cornell University Medical College.

1. Lewis, G. M.; Montgomery, R. M., and Hopper, M. E.: Cutaneous Manifestations of Trichophyton Purpureum (Bang), Arch. Dermat. & Syph. **37**:823 (May) 1938.

but with the desire that the faint possibility of a fungous disease be ruled out. The direct mount and culture methods both gave positive results in 292 cases. In an additional 108 cases pathogenic fungi were found in the direct mount but no growth appeared on the culture medium. Each patient was examined for other evidence of fungous disease besides the condition for which he sought relief. It is of interest that in 23 instances we obtained proof of the simultaneous or successive presence of two or more different species of pathogenic fungi which were considered to be causing a mycotic infection of the skin. In the majority of the cases there seemed to be no relation clinically or immunologically between the different manifestations of disease and the fungi which were isolated from different parts of the body. This group of cases we have included as instances of "concurrent infection," while "combined infection" refers to the condition in the fewer cases in which isolation of fungi from the same area of skin caused us to suspect a clinical or immunologic interrelation. In one instance a fungous infection due to one pathogen clearly antedated a second fungous infection due to a species different from the first. We refer to such an infection as "consecutive." Such terms are useful as possible explanations of the cultural findings. In practice, one is not always able to decide which category best fits the particular case. In this study, fungi of doubtful or infrequent pathogenicity are not included. The cases summarized here are arranged according to the various combinations of fungi which were isolated.

REPORT OF CASES

TRICHOPHYTON GYPSEUM AND TRICHOPHYTON PURPUREUM

CASE 1.—G. V., a 33 year old Puerto Rican, a clerk, had an infection of the skin and nails of his hands and feet for over eleven years. The clinical appearance was suggestive of a T. purpureum infection, but there was more inflammation than is usually seen. T. gypseum was isolated from material from the toes and toe nails, while T. purpureum grew from scrapings from the finger nails. A month later, and coincident with clinical improvement, only T. purpureum could be isolated from the various affected tissues. Prolonged or intensive treatment is known to alter the findings on culture. T. purpureum resists treatment, whereas therapy may cause T. gypseum to disappear.

TRICHOPHYTON GYPSEUM, TRICHOPHYTON PURPUREUM AND MALASSEZIA FURFUR

CASE 2.—P. R., a boy aged 15, presented himself for the treatment of scabies. Sarcoptes scabiei was demonstrated. In the routine examination a brownish scaly area was noted on the right shin. M. furfur was demonstrated in this site. There were also some scaling and maceration between the toes; on culture, T. purpureum was isolated. Two months later, during the early summer, T. gypseum was grown from material taken from the feet. This case illustrates (1) a concurrent nonrelated infection of tinea versicolor and dermatophytosis and (2) a seasonal change in the flora of tinea pedis, with T. gypseum infection appearing during the hot months.

TRICHOPHYTON GYPSEUM AND EPIDERMOPHYTON INGUINALE

CASE 3.—P. A. S., a man aged 30, entered the hospital for the treatment of a gunshot wound. While he was in the hospital during the summer, a tinea infection developed on his feet, with erythema, scaling and edema. E. inguinale was isolated from material from his left foot and T. gypseum from the right. The acquisition of the infection was attributed to walking barefoot in the bathroom and in the pavilion.

TRICHOPYTON GYPSEUM AND MONILIA ALBICANS

CASE 4.—F. K., a woman aged 48, a housewife, had a chronic paronychia of the right middle finger recurrent for the past eight years. For about the same time she had gradually increasing disability of the feet. The skin of the soles was thickened, dry and scaly. Some interdigital maceration was present. All the toe nails were yellow, friable and opaque. M. albicans was isolated from the area of chronic paronychia. T. gypseum was grown from material from the toes and toe nails.

CASE 5.—V. E., a woman aged 45, a housewife, had recurrent paronychia of several fingers with resultant infection of the nails of the affected digits. She had occasional spells of itching between the toes. One year previously she had noticed some fissures at the angles of the mouth. The examination showed a subacute tinea pedis with redness, scaling and maceration of the last two webs of both feet. Three fingers showed chronic paronychia and typical involvement of the nails. The tongue was red, and a commissural intertrigo was noted at the angles of the mouth. T. gypseum was grown from material from the toes and toe nails and M. albicans from the finger nails, tongue and angles of the mouth.

CASE 6.—F. M., a woman aged 35, a housewife, complained of vulvar pruritus of eight months' duration. There was a moist, soggy, intertriginous infection of the groin, from which M. albicans was isolated. The toe webs were mildly inflamed and scaly, and on culture T. gypseum was isolated.

CASE 7.—F. K., a woman aged 51, a housewife, had chronic paronychia for seven years. A slide and culture revealed M. albicans. A mildly inflamed eruption of the feet yielded T. gypseum on culture.

CASE 8.—B. S., a woman aged 63, a housewife, had had recurrent attacks of an eruption on her hands and feet during the past thirty-eight years. She also had had a rash in the inframammary and inguinal regions for several years. The skin of several interdigital webs of the feet showed maceration and redness. Vesicular and scaly patches were present on the palms and sides of the fingers. Intertriginous red and well defined plaques were present in the inframammary and inguinal regions. The mycologic examination resulted in cultural demonstration of T. gypseum in material from the feet and of M. albicans in a specimen from the inframammary region. No fungi were found in material from the hands.

TRICHOPHYTON GYPSEUM AND MALASSEZIA FURFUR

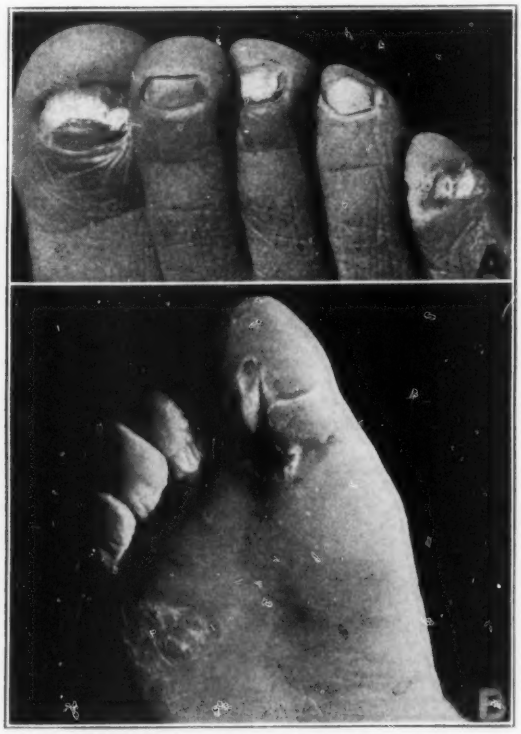
CASE 9.—R. S., a spinster aged 54, had recurrent attacks of tinea versicolor, for which she received local applications. In the routine examination of her skin, some material from macerated areas between the toes was cultured, yielding a growth of T. gypseum.

CASE 10.—I. M., a man aged 45, a chauffeur, came to the clinic because of an eruption on his hands. There were a scaly eruption on the sides of the fingers

and interdigital scaling of the feet. A brownish, scaly eruption on the body had been noted for the past year. T. gypseum was isolated from the toes and M. furfur from the body lesions.

TRICHOPHYTON PURPUREUM AND EPIDERMOPHYTON INGUINALE

CASE 11.—N. K., a man aged 35, a railway clerk, had a yellowish, opaque, thickened and friable left thumb nail. There were maceration, scaling and fissuring of the webs of the toes. T. purpureum was isolated from the thumb nail. E. inguinale grew from scrapings from the webs of the toes.



Involvement of the nails and skin due to different fungi (case 12): (*A*) onychomycosis due to Trichophyton purpureum and (*B*) subacute dermatophytosis caused by Epidermophyton inguinale.

CASE 12.—W. C., a Chinese man aged 34, a kitchen worker, had clinical evidence of chronic tinea of the toes and of the toe nails. Cultures of material from both sites resulted in the growth of T. purpureum from the nails and of E. inguinale from the sides of the toes.

CASE 13.—E. B., a youth aged 20, a student, suffered from hyperkeratosis affecting his soles since he was an infant. For several years he had noticed scaling between the toes and thickening of the toe nails. Over the instep there were inflamed and scaly areas. Culture of material from one of his soles showed E. inguinale and from the toe nails T. purpureum.

CASE 14.—T. F., a man aged 23, a medical student, was first seen in the summer of 1939, when he had a vesicular eruption limited to the palms and soles. This cleared spontaneously, as had previous attacks during the last six years. In recurrence in April 1940 the results of laboratory tests were negative. There was no reaction to trichophytin. Subsequently he was seen for scaly eruptions of the feet, hands and groin, in February 1941, when T. purpureum was recovered in material from his feet, and in May 1941, when E. inguinale was grown from material from the soles but no growth was obtained from the hands or groin.

TRICHOPHYTON PURPUREUM, EPIDERMOPHYTON INGUINALE AND TRICHOPHYTON GYPSEUM

CASE 15.—M. W., a man aged 45, a traveling salesman, complained of a pruritic, well demarcated, reddened, scaly plaque on the upper and inner parts of the left thigh. Material from this area grew T. purpureum. There were some interdigital maceration of the toes and some scaling of the left sole. T. gypseum was isolated from the webs of the right foot and E. inguinale from the left sole.

Occupation may allow a person to come in contact with pathogenic fungi. Traveling and living in hotels were probably responsible in this case.

TRICHOPHYTON PURPUREUM AND MONILIA ALBICANS

The clinical signs of chronic ringworm of the feet, hands or groin are often complicated by the presence of soggy or macerative tissue. Many of the patients have received treatment. The first mycologic examination frequently yields M. albicans alone. After treatment and on further examination the underlying and probably the primary infective agent will be found to be T. purpureum.

CASE 16.—E. D., a woman aged 67, a practical nurse, was born in Jamaica, West Indies, and was still living there when she first noticed an infection of the feet twenty years before. She had been to many physicians and clinics for treatment. The ankles and legs also were affected. The affected skin was reddened, scaly and infiltrated, resembling neurodermatitis. The clinical impression was dermatophytosis due to T. purpureum. Cultures on four occasions resulted in the finding of M. albicans, which did not correspond with the appearance of the disease. On one of the dried cultures, however, a fluffy growth was noted which on subculture was identified as T. purpureum.

CASE 17.—M. V., a woman aged 23, a technician, had a chronic, erythematous scaly condition on the sides of the feet and soles with involvement of the toe nails for over two years. On direct examination filamentous fungi were present. The culture grew M. albicans. After the yeastlike growth had stood for over a month T. purpureum appeared.

CASE 18.—J. H., a man aged 24, an accountant, presented himself for treatment of a pruritic, dry, red, scaly and slightly infiltrated eruption on the upper and inner parts of the thighs and in the intergluteal fold. Some maceration with scaling was present on the toe webs. A ringed, quarter-sized, dull red, scaly plaque was noted on the right side of the chest. Cultures of material from the

chest grew T. purpureum. M. albicans developed in the culture from the groin. Bacterial overgrowth in the culture tubes prevented any fungi from developing in specimens from the feet. Clinically, the eruption in the groin and feet suggested a T. purpureum infection, and it is our belief that if repeated cultures had been possible T. purpureum would eventually have been grown.

CASE 19.—L. H., a woman aged 49, a housewife, came to the clinic for treatment of chronic paronychia and onychia of several fingers present for fourteen months. M. albicans was cultured from scrapings from the nails. Cultures of materials from the toes, where there were scaling and maceration, revealed T. purpureum. This is a not uncommon finding of two concurrent and wholly unrelated infections.

TRICHOPHYTON PURPUREUM AND MALASSEZIA FURFUR

CASE 20.—M. H., a man aged 32, unemployed, stated that a well demarcated, thickened, scaly, red plaque in his right groin had been present for three years. There was intense pruritus sporadically. T. purpureum was grown from scrapings of this patch in the right groin and also from the webs of his toes, invaded toe nails and thickened soles. M. furfur was present in material scraped from superficial brown scaly lesions on the trunk.

EPIDERMOPHYTON INGUINALE AND MALASSEZIA FURFUR

With both fungi the resultant cutaneous infection is apt to be macular and scaly, but with E. inguinale there is usually more redness. Some clinical confusion may result when the condition is localized to intertriginous locations.

CASE 21.—E. P., a man aged 24, a fireman, had a brownish, scaly macular eruption over the pubis, in the inguinal region and on the upper and inner parts of the thighs. There was minimal scaly involvement of the webs of the toes. M. furfur was demonstrated in scrapings from the inguinal region. E. inguinale was isolated from the lesions of the toes.

MONILIA ALBICANS AND MICROSPORON MINUTISSIMUM

CASE 22.—R. P., a 43 year old Italian woman, a housewife, presented a sharply defined, intertriginous, slightly erythematous, scaly eruption involving the axillas, the inframammary regions, the region around the umbilicus and the inguinal and intergluteal regions. M. minutissimum was demonstrated in material from these locations. There was sodden, macerated skin on two interdigital webs of the hands, from which M. albicans was isolated and considered to be of pathogenic importance.

MALASSEZIA FURFUR AND MICROSPORON MINUTISSIMUM

CASE 23.—S. S., a man aged 60, unemployed, had irregular, brown, scaly lesions scattered over the trunk, from which M. furfur was readily isolated. Larger plaques were present in either axilla from which M. minutissimum was demonstrated. A year later the patient returned; the condition was noted to be practically unchanged, and the laboratory findings were the same.

REVIEW OF THE LITERATURE

In a recent report, Muskatblit [2] brought the subject of multiple fungous infections up to date. He found evidence of only 36 cases in the literature, and with the 6 cases which he described this made a total of only 42 cases in which more than one pathogenic fungus had been isolated. It is of interest that in 21 of 37 cases for which data are available the scalp was the only site of the infection and in 4 other cases it was one of two sites. In the cases which we describe in this paper no multiple infections of the scalp were noted nor was the scalp one of the sites involved. In addition to the combinations of fungous infections mentioned in Muskatblit's paper, we are able to report as original observations seven new multiple infections, due to: (1) Trichophyton gypseum, Trichophyton purpureum and Malassezia furfur in all four combinations; (2) Trichophyton gypseum, Trichophyton purpureum and Epidermophyton inguinale; (3) Epidermophyton inguinale and Malassezia furfur; (4) Monilia albicans and Microsporon minutissimum.

TABLE 1. —*Results of the Trichophytin Test in Seventeen Cases of Multiple Fungous Infections* *

Case	Reaction: Fifteen Min.	Reaction: Forty-Eight Hr.	Trichophyton gypseum	Trichophytor purpureum	Epidermophyton inguinale	Monilia albicans	Malassezia furfur	Microsporon minutissimum
1	—	+	+	+	..	..	..	..
2	—	—	+	+	..	..	+	..
3	—	—	+	..	+	..	..	..
4	—	+	+	..	..	+	..	..
5	—	+	+	..	..	+	..	..
6	—	±	+	..	..	+	..	..
7	—	++	+	..	..	+	..	..
8	—	+	+	..	..	+	..	..
9	—	++	+	..	..	..	+	..
10	—	+	+	..	..	..	+	..
11	+	—	..	+	+	..	..	..
12	±	±	..	+	+	..	..	..
13	+	+	..	+	+	..	..	..
14	—	±	..	+	+	..	..	..
15	—	—	+	+	+	..	..	..
16	+	—	..	+	..	+	..	..
17	—	—	..	+	..	+	..	..
18	+	+	..	+	..	+	..	..
19	—	—	..	+	..	+	..	..
20	++	—	..	+	..	..	+	..
21	—	+	..	..	+	..	+	..
22	—	—	..	..	..	+	..	+
23	—	—	..	..	..	..	+	+

* In six instances the results were unknown or not available.

2. Muskatblit, E.: Combined Fungous Infections: Report of Six Cases with a Review of Thirty-Six Cases from the Literature, Arch. Dermat. & Syph. **44**:631 (Oct.) 1941.

COMMENT

The average age of our patients was 39. There were 13 males and 10 females. A striking clinical feature was the slight degree of inflammation, indicating that the patient's skin was not sensitized deeply. The trichophytin test did not uncover any strong reactions. In 2 cases there were both an immediate wheal reaction and a delayed (tuberculin type) reaction to trichophytin. In the cases in which Trichophyton purpureum was isolated, cure was as difficult as in cases in which this was the only micro-organism present.

TABLE 2.— *Estimation of the Type of Multiple Fungous Infection in the Cases Reported in this Paper*

Case	Concurrent	Combined	Consecutive
1	..	+	..
2	+	..	+
3	+	..	..
4	+	..	..
5	+	..	..
6	+	..	..
7	+	..	..
8	+	..	..
9	+	..	..
10	+	..	..
11	+?	+?	..
12	+	+?	..
13	+?	+?	..
14	..	+	..
15	+	+?	..
16	..	+	..
17	..	+	..
18	+?	+?	..
19	+	..	..
20	+	..	..
21	+	..	..
22	+	..	..
23	+	..	..

In reviewing our cases, we encountered difficulty in establishing primary and secondary roles for the fungi which we isolated or in deciding the possibility of symbiotic effects between them. We believe that immunologic studies are of limited value except when changes in the allergic state can be demonstrated coincidental with changes in the fungus flora. As mentioned previously, the literature on this subject is scanty. It is our opinion that the paucity of reports or of cases in which more than one pathogenic fungus has been isolated is really not a true index of the actual state of affairs. When we have seized the opportunity of reexamining patients, there has been a striking increase in our positive results and in the number of cases in which double or triple infections have been found to be present. We were able to find these cases mainly because of the close cooperation between the clinic and laboratory which exists in the dermatologic department at the New York Hospital.

SUMMARY

Twenty-three cases of multiple fungous infections are reported. Difficulty was encountered in deciding the role of the pathogenic species isolated from diseased tissue. Immunologic studies in 17 cases did not provide much help in establishing the primary infective agent. In only 1 case was there sufficient evidence to justify considering the infections "consecutive." Nine of the patients (5 being doubtful) were considered to have combined infections in which the species of fungi were working together. In 19 cases (3 being doubtful) evidence of concurrent (unrelated) fungous diseases was present. It is thought that cases of multiple fungous infections are not uncommon. More cases would come to light if repeated laboratory studies were undertaken, particularly at widely spaced intervals, and if the patients received complete clinical examinations of both suggestive locations and parts of the body not often involved. Seven new combinations of multiple fungous infections are reported in this paper.

121 East Sixtieth Street.

DERMATITIS VENENATA CAUSED BY THE MANZANILLO TREE

CAPTAIN EMANUEL M. SATULSKY
MEDICAL CORPS, UNITED STATES ARMY

Hippomane mancinella L., family Euphorbiaceae, is a poisonous tree which is found on both sides of the isthmus and commonly along the seashores throughout Panama and the Canal Zone. It often forms dense thickets along the beaches and is easy to recognize. The common name is the manzanillo tree; the names beach apple and shore apple are more recent ones.

It is a large branching tree characterized by a smooth gray bark, which may also have a pale brown hue, and by dense foliage. The fruit is bright red and more than an inch (2.5 cm.) in diameter and resembles a green apple in shape. The leaves are alternate, long petioled, broadly ovate, finely serrate and dark green and are similar in shape to those of a cherry tree. They are usually turned to the right at the tip. The flowers are green and are arranged in stiff spikes.

The fruit, leaves and branches when cut or bruised exude a milky latex which is highly irritant, causing severe inflammation and vesiculation of the skin. The type of eruption is similar to that produced by Rhus toxicodendron and other irritant plants. It is extremely irritating to the mucous membranes, particularly the conjunctivas. If the leaf or the fruit is eaten, such a severe edema of the throat, esophagus and digestive tract occurs that tracheotomy may be required to save life. Soldiers have been known to use the leaves for toilet paper, with disastrous results to the perianal areas, the mucous membrane of the anal orifice and other adjacent parts.

Directions are published each year by the office of the Department Surgeon relative to manzanillo poisoning,[1] and similar reference to poisoning by this tree may be found in the "Manual on Jungle Warfare." Information regarding this tree has been disseminated to the military personnel of this department. Soldiers are repeatedly cautioned not to bite the fruit, to avoid contact with the tree in any way, not to use

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1. Circular 61, Headquarters Panama Canal Department, April 8, 1942.

the leaves or the branches for bedding and not to sleep under these trees. It is reported that the sap of this tree is so poisonous that the dew falling from it and coming into contact with the skin will cause grave irritation. The natives have known for a long time that a person sleeping under the manzanillo tree will surely awaken "all swollen up." The Department Surgeon's office has stated: [2]

> The so-called "swelling up" of persons who may sleep under manzanillo trees is not a superstition but a fact, since hypersensitive persons suffer from edema of the eyelids and puffiness of the face without direct contact with the leaves, fruit or bark of this tree. Dew falling from the leaves contains sufficient toxin to cause irritation and edema in hypersusceptible individuals.

From the Bureau of Entomology and Plant Quarantine of the United States Department of Agriculture [3] it has been reported that there is a simple and very effective remedy always at hand, i. e. sea water. Immersion of the body or the affected part in salt water (sea water) for one-half hour is helpful and relieves the majority of the symptoms. This has been used in the Panama Canal Department for years. Men coming into contact with the manzanillo tree are instructed to plunge into the sea and remain there for thirty minutes.

This agency also reports that the Euphorbiaceae are known to have many bad actors among them. A common one is Hura crepitans L., a rather common tree in the zone. It is known as the javille or sand-box and is of medium size. The trunk usually is covered with sharp spines. The leaves are long petioled, cordate-ovate and toothed. The fruit is a capsule 8 to 10 cm. in width, shaped like a flattened pumpkin, with about fifteen one-seeded woody cells which resemble orange segments. When ripe, the fruit explodes, scattering the seeds for some distance. The seeds contain an oil which has drastic purgative qualities and also induces vomiting. It is used to poison animals. The sap is milky and is also poisonous, causing severe dermatitis on contact with the skin. The sap mixed with meal is thrown into water to stupefy fish.

In the genus Sapium there are at least two species, both trees, with a milky sap which is said to act much like that of Hippomane. It is much more sticky, and some South American species are good sources of a commercial rubber. The common name here is *olivo,* or *ñipe.*

It is interesting to note that the common weed Euphorbia hirta, whose common name is *hierba de polle,* has a bad reputation in Panama. It is called milkweed by the Jamaicans but is not a true milkweed. It was formerly believed to harbor the organism of tropical ulcer, but the Spirilla found in its sap have never been proved to cause ulcus tropicum.

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2. Personal communication to the author from the office of the Departmental Surgeon.

3. Zetek, J., entomologist, United States Dept. of Agriculture: Personal communication to the author.

I wish to report a case of dermatitis venenata caused by contact with the beach apple, shore apple or manzanillo tree. It is realized that a scientifically definite diagnosis cannot be made without patch tests with the bark, fruit, leaves, etc., directly. It must be remembered, however, that the function of the Medical Corps is to return patients to duty with the least possible delay and as efficiently as possible. It was felt that the additional hospitalization and the possibility of producing an acute, widespread, incapacitating flare-up were not justified at the present time. This case is reported because of general interest. As stated previously, each year the Department Surgeon publishes a warning relative to the hazards of contact with the manzanillo tree, yet in the United States dermatologists are not too familiar with them.

REPORT OF A CASE

E. D. S., a 28 year old white soldier, was admitted to the hospital because of edema of the prepuce, a small penile ulceration and an eruption of the skin. His past history was noncontributory. He stated that he and the members of his outfit had been warned about coming into contact with this tree. About April 2, 1942 he came into contact with a manzanillo tree while in the course of his duties. He was wearing fatigue clothes, the shirt of which was open. He was unable to wash his hands for several hours and during this time handled his penis several times during urination. After the exposure he immediately felt a sensation "like tear gas burning my skin." Other men in his outfit suffered from the same type of eruption, but he was sent into the hospital because of the penile abrasion and the edema of the penis. He reported that the natives had cautioned the soldiers about the dangers of this tree.

Examination revealed a mild edema of the prepuce, and a pinpoint-sized, superficial abrasion of the prepuce on the right side at the mucocutaneous junction. There was no induration and no adenopathy. He had an erythematous macular and small papulovesicular eruption on the lower part of the abdomen, about the umbilicus, on the lower part of the chest and on the thighs. His main complaint was pruritus. The thighs showed scaliness, and the eruption seemed to be fading. Here there were many follicular minute pustules with some erythematous macules scattered over the entire anterior surfaces. There was a mild edema of the scrotal sac. The patient stated that he had previously had redness of the face and the backs of the hands.

Dark field examinations of the superficial ulceration were made on two successive days and failed to show Spirochaeta pallida. The Kahn and Wassermann reactions of the blood were negative. A blood cell count showed: red cells 4,200,000 and white cells 7,750, with polymorphonuclear leukocytes 60 per cent, lymphocytes 34 per cent and eosinophils 6 per cent. The hemoglobin content (Sahli) was 90 per cent. The urine was normal. The remainder of the physical examination gave essentially normal results.

After the use of warm saline solution dressings, the edema of the penis and scrotum subsided, the penile ulceration healed, the cutaneous eruption regressed and the patient was discharged to duty, five days after admission.

SUMMARY

1. Report is made of the irritating actions of the manzanillo (beach apple or shore apple) tree found in Panama and the Canal Zone.

2. A report is submitted of a soldier who had dermatitis venenata after exposure to this tree.

3. An effective method of therapy is immersion of the body or of the affected part in sea water (salt water) for half an hour.

4. Soldiers have been repeatedly warned against exposure, and the Department Surgeon has issued warnings relative to the dangers of this tree to all the personnel in this department.

Elizabeth, N. J.

ACETARSONE IN THE TREATMENT OF PEMPHIGUS

M. OPPENHEIM, M.D.
AND
D. COHEN, M.D.
CHICAGO

At the meeting of the Vienese Dermatological Society in November 1927 one of us (M. O.)[1] presented a patient with pemphigus serpiginosus who had been treated with acetarsone. This was a 58 year old woman who had an eruption of three and one-half months' duration. Acetarsone and exposure to ultraviolet radiation from a quartz mercury vapor lamp caused improvement with a tendency toward epithelization.

After this demonstration several cases of eruptions of the pemphigus group were published in which the disease was favorably influenced by acetarsone. Kromayer[2] in 1929 reported 6 cases of pemphigus, including 2 in which it was severe, in which the eruption was healed. The drug was administered over a long period with intermissions. In 1 case 600 tablets were given. All the patients improved so that they were able to return to their former occupations. Relapses in the form of blisters and in 1 case of red, scaly macules subsequently disappeared. His conclusion was that pemphigus is deprived of its acute character by treatment with acetarsone and assumes a chronic inflammatory type. This improvement bordering on complete healing took place in a disease which otherwise nearly always ends fatally.

Vamos[3] in 1929 described 2 patients with pemphigus from Nekam's clinic; 1 had pemphigus vegetans and was given 190 tablets, and the other received 160 tablets, with decided improvement. Brann[4] in 1929 and Langer[5] and Freund and Mueller[6] in 1930 reported success with acetarsone in the treatment of pemphigus vulgaris.

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1. Oppenheim, M.: Pemphigus chronicus serpiginosus, Zentralbl. f. Haut- u. Geschlechtskr. **26**:350, 1927.

2. Kromayer, E.: Sechs durch Spirozid geheilte Pemphigusfälle, Deutsche med. Wchnschr. **55**:229-230, 1929.

3. Vamos, L.: Pemphigus vegetans, Zentralbl. f. Haut- u. Geschlechtskr. **32**: 791, 1929; Mit Spirozid geheilter Pemphigus, ibid. **34**:22, 1930.

4. Brann: Zwei Fälle Pemphigus vulgaris, Zentralbl. f. Haut- u. Geschlechtskr. **32**:557, 1929.

5. Langer, E.: Pemphigus vulgaris: II. Pemphigus vegetans, Zentralbl. f. Haut- u. Geschlechtskr. **33**:301, 1930.

6. Freund and Mueller: Pemphigus vulgaris, Zentralbl. f. Haut- u. Geschlechtskr. **34**:531, 1930.

7. Footnote deleted on proof.

In a paper discussing the entire subject, one of us (M. O.) [8] described 4 patients with pemphigus and 1 with dermatitis herpetiformis who were treated with this drug with excellent results. Three of these had severe involvement of the mucous membranes of the mouth and 1 of the vaginal mucosa. All were discharged without symptoms or greatly improved. From these observations it was concluded that it was justifiable to try acetarsone in the treatment of pemphigus, the drug to be given as early as possible for a long period in sufficient dosage, of course only under the most exact medical supervision. It was also thought important to prevent parenteral absorption from erosions in the mouth by administration of the drug in capsules.

At a meeting of the Chicago Dermatological Society Rothman [9] stated:

> Acetarsone, which was first used by Oppenheim, is one of the most potent chemotherapeutic drugs in the therapy of pemphigus. Through its use the life expectancy of patients with pemphigus becomes twice as long, on the average. The fatal outcome can only be deferred by acetarsone, as well as by germanin; acetarsone is the less toxic drug.

At various meetings of the Chicago Dermatological Society, we presented 3 patients with pemphigus, including 2 with pemphigus vulgaris and 1 with pemphigus vegetans. All were treated with acetarsone. These patients are symptomless after more than one year. They are referred to in our paper on "Primary Lesions of Pemphigus Vulgaris." [10] Our first patient when seen was in a serious condition. He was given six blood transfusions and one course of germanin therapy and has taken about 200 tablets of acetarsone. Locally, the lesions were debrided and 5 per cent boric acid ointment applied. The second patient had one transfusion and now has taken 181 tablets. The third patient improved so promptly after administration of acetarsone that it was possible to omit transfusions. She has now taken about 146 tablets. Since our presentations, other patients with pemphigus vulgaris have been presented before the Chicago Dermatological Society by Ebert [11] and Zakon,[12] with decided improvement due to treatment with acetarsone.

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8. Oppenheim, M.: Ueber die Verwendung des Spirocids beim Pemphigus vulgaris chronicus und vegetans nebst Bemerkungen zur Spirocidtherapie, Dermat. Wchnschr. **91**:1855, 1930.

9. Rothman, S., in discussion on Rattner, H., and Cornbleet, T.: A Case for Diagnosis (Bullous Eruption), Arch. Dermat. & Syph. **43**:1061 (June) 1941.

10. Oppenheim, M., and Cohen, D.: Primary Lesions of Pemphigus Vulgaris, Arch. Dermat. & Syph. **46**:201 (Aug.) 1942.

11. Ebert, M. H.: Pemphigus Vulgaris Treated with Acetarsone, Arch. Dermat. & Syph. **45**:796 (April) 1942.

12. Zakon, S. J.: Pemphigus Erythematodes (Senear-Usher), Arch. Dermat. & Syph. **45**:791 (April) 1942.

Our method of treatment is as follows: The acetarsone is given every morning, one-half hour before breakfast, for three consecutive days. This is followed by a rest period of three days, after which treatment is again resumed. The dose is 8 tablets given in three mornings: 2 tablets the first morning and 3 tablets each of the remaining two mornings. The tablets are dissolved in a small amount of water, and after taking this the patient drinks a half-glassful of water. The patient takes 2 Gm. of acetarsone in three days, and then there is a three day rest period. If one is apprehensive regarding the toleration of the drug, 1 tablet is given every morning for the first three days and then 2 tablets for the second three day period (following the rest period) and finally the maintenance doses of 2, 3 and 3 tablets. This dosage is maintained until the number of tablets taken equals the number of kilograms of body weight. We then continue the administration with longer intermissions and with lessening of the dosage following clinical and subjective symptoms. At the moment that the patient feels ill or if pruritus appears, administration of the drug is stopped. When these symptoms disappear we begin again with 1 tablet every morning for three days, and after three days' rest the dose is increased slowly up to 8 tablets in three days. If the epithelium of the mouth is not intact, acetarsone tablets are pulverized and administered in capsules to prevent parenteral absorption. In no case do we neglect the usual treatment of pemphigus. Two of our patients received blood transfusions, and 1 of these also was given a series of germanin treatments. All 3 of them were given vitamin B complex. Locally daily oatmeal baths and 5 per cent boric acid ointment were used, and a bland diet was prescribed.

SUMMARY AND CONCLUSIONS

In 3 cases of pemphigus, including 1 of pemphigus vegetans, there was decided improvement bordering on healing from the administration of acetarsone. In spite of the large amount of acetarsone administered, no untoward effects were observed. The clinical aspect of the acute bullous eruption is sometimes changed to that of chronic urticaria papulosa or impetigo. In every case of pemphigus a trial with acetarsone should be made, as early as possible.

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SHOCK-PROOF ROENTGEN RAY APPARATUS IN DERMATOLOGY

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Shock-proof x-ray apparatus have been used by dermatologists and radiologists for several years. Leading manufacturers in the United States now furnish only this type of apparatus. This indicates the obvious advantages of shock-proof x-ray machines. The purpose of this communication is twofold: first, to relate the differences in technic between use of shock-proof and that of nonprotected apparatus in treating diseases of the skin and, second, to describe the field of irradiation and the physical characteristics of the emitted x-ray beam of the newer machines. Shock-proof apparatus are safer than the older types; nevertheless, certain precautions are necessary for their safe use. No machine is foolproof.

DESCRIPTION OF APPARATUS

A shock-proof x-ray machine consists essentially of an autotransformer, a high tension transformer, a valve tube rectifier, a filament heating transformer and an appropriate panel board containing the meters, switches and regulating devices. These elements are contained in most x-ray apparatus. The features of difference in the shock-proof machine are in the connecting cables and the tube housing. The connecting cables and the tube ends were formerly unprotected, and a person coming in contact with them received a severe electrical shock. Now the connecting cables in a shock-proof apparatus consist of flexible copper wires which are insulated with a rubber material, and surrounding this is a grounded metal sheath. This type of cable prevents electrical shock even though a patient or bystander may come in direct contact with it.

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The tube is surrounded by a metal enclosure provided with a window which is made of a material transparent to roentgen rays. The space between the metal casing and the tube is filled with oil, and the oil is cooled either by a suitable apparatus which forces circulation of the oil through a cooling device or by coils through which cool water is circulating. The x-ray tube is made up of essentially the same component parts as the old fashioned Coolidge tube, except that it is greatly reduced in size. The target varies considerably, however, in that the solid tungsten target of the old Coolidge tube was tilted at an angle of 45 degrees, whereas the copper-backed anode of the newer tubes is tilted to a lesser angle. The average angle is between 20 and 30 degrees. The

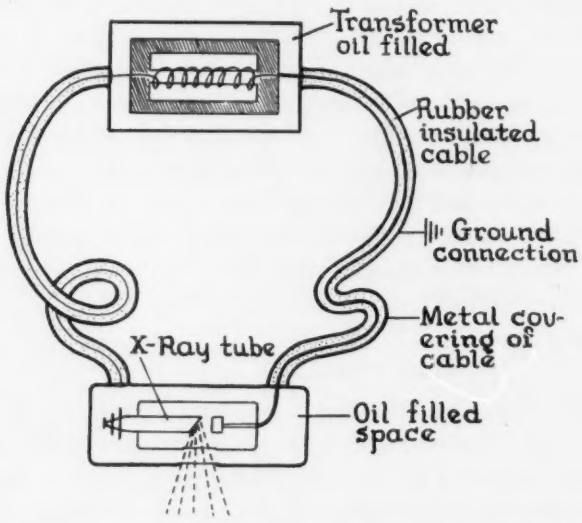

Fig. 1.—The tube housing, high tension transformer housing and flexible connecting cables are thoroughly grounded, electric shock thereby being prevented.

roentgen rays after striking the target pass through the glass envelope and then have to penetrate a layer of oil and finally go through the window of the tube housing before striking the skin. The newer tubes are almost all made of pyrex glass.

The complete tube with its housing is somewhat heavier than the formerly used glass bowl or leaded box and therefore requires more elaborate balancing devices for adequate flexibility, so that lesions, no matter where they may be located on the surface of the body, can easily be reached. Wooden tables, which were formerly used for protective purposes, are not necessary with shock-proof apparatus.

The apparatus which is best suited for dermatologic work, including the treatment of most malignant lesions of the skin, is the type which

produces from 50 to about 140 kilovolts. The modern tube housing not only prevents electrical shock but also is roentgen ray protective. In other words, this apparatus permits roentgen rays to issue from the tube only through the window provided for this specific purpose. Suitable filters and cones and devices for measuring skin-anode distances, for centering and proper angulations, add to the flexibility of modern shock-proof roentgen ray machines.

THE QUALITY OF RADIATION EMITTED BY SHOCK-PROOF APPARATUS DESIGNED FOR DERMATOLOGIC THERAPY

Because roentgen rays generated in shock-proof apparatus have to traverse oil and two windows, it is generally assumed that the emitted rays are harder than those ordinarily obtained from the old type tube. Experiments were conducted with several types of apparatus at our disposal to determine exactly the half value layer of the roentgen ray beam emitted from the old type apparatus with a universal Coolidge tube. The half value layer of the radiation from a modern shock-proof apparatus was obtained, and the two were compared. The half value layers were determined both with the universal type Coolidge tube made of pyrex glass and with the soft thin-walled glass bulbs. The usual physical procedures for determining the half value layer were followed, and the half value layer was found to be 0.88 mm. of aluminum, using a universal Coolidge pyrex tube, no filter and 100 kilovolts. With the thin-walled soft glass universal Coolidge tube the half value layer was found to be 0.26 mm. of aluminum. The half value layer obtained with the shock-proof apparatus which is installed at our clinic was found to be 0.80 mm. of aluminum. It is understood that there was no additional filter and the kilovoltage was 100. The Universal Coolidge tubes manufactured within the last few years have pyrex glass bulbs. It can therefore be seen that the half value layer of unfiltered roentgen rays from a modern universal Coolidge tube is about the same as that from a modern shock-proof apparatus. The quality measurements of the rays from the two types of modern apparatus are so close together that there is little physical difference and practically no biologic difference, so far as we were able to determine with erythema dose tests.[1]

It has been generally believed by dermatologists that roentgen rays from shock-proof apparatus were so hard that they were equivalent to those obtained through 0.5 mm. of aluminum. Our experiments conclusively indicate that the quality of radiation obtained from modern

1. The ionization instruments used for making the determinations were the Wulf and Victoreen ionometers calibrated for rays at various wavelengths and in particular at long wavelengths.

shock-proof x-ray apparatus at 100 kilovolts is not harder than a beam of roentgen rays obtained with nonprotected x-ray machines with modern universal Coolidge tubes.[2]

Because the quality of the rays emitted from the shock-proof apparatus is practically the same as that emitted from the unprotected apparatus, the number of roentgens required to produce an erythema when equivalent voltages and filters are used is also about the same. We therefore advocate that 300 r as measured routinely with a portable thimble type ionization instrument and a fixed scale in roentgens be used for the erythema dose of unfiltered radiation. For filtered radiation at 120 to 140 kilovolts we recommend that 400 r be used as the erythema dose when 0.5 mm. of aluminum is used, 450 r when 1 mm. of aluminum is used and 550 r when 3 mm. of aluminum is used.[3]

THE FIELD OF DISTRIBUTION OF ROENTGEN RADIATION

In treating cutaneous lesions it is often necessary to expose large surfaces of the body. In any one day not more than a third or a fourth of the body surface should be irradiated. In the treatment of large surfaces, considerable time is consumed. Therefore, in order to save time and to irradiate large areas adequately and uniformly it is necessary to employ the principle of overlapping. There are certain objection to this method which we shall not discuss at this time. However, experience definitely indicates the safety of the overlapping technic when it is properly carried out. In fact, the five point Kienböck-Adamson technic for temporary epilation of the scalp of children afflicted with tinea is the best example of the overlapping principle.[4] In order to employ successfully and safely the overlapping technic it is necessary that the apparatus emit roentgen rays which are uniformly distributed over a plane surface and follow the inverse square law. A universal Coolidge x-ray tube with the target angulated at 45 degrees and with a round focus spot provides a distribution which is uniform in substantially all directions from the central point. In other words, assuming that the intensity of a beam is measured beginning from the center and in a plane at right angles to this center beam, the intensity toward the border decreases

2. Cipollaro, A. C., and Mutscheller, A.: Absorption of Roentgen Rays by the Skin: Experimental Determinations, Arch. Dermat. & Syph. **41**:87-95 (Jan.) 1940.

3. A word of warning should be interjected at this point. All apparatus are not manufactured alike, and therefore the figures which we have obtained with the materials and machines at our disposal may not apply in all instances. It is well that each apparatus be calibrated by a physicist before it is put to clinical use. (MacKee, G. M., and Cipollaro, A. C.: The Roentgen Unit in Dermatology, Arch. Dermat. & Syph. **30**:761-767 [Dec.] 1934; Roentgen Dosage in Dermatology Expressed in International Roentgens, ibid. **41**:1-7 [Jan.] 1940).

4. MacKee, G. M.: X-Rays and Radium in the Treatment of Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1938.

inversely as the square of the distance. This, therefore, makes it possible to calculate accurately the amount of radiation falling on any point at a given distance from the center. When the adjacent area is treated, by measuring the distance between the center of the target and the skin, one can determine how much of the radiation falls on any point away from the center. The shock-proof apparatus which we tested revealed that the field of distribution is not uniform. We find that the inverse square law does not apply to all radial distances from the center. The falling off of the intensity is greater than that corresponding to the inverse square law.

For example, if in figure 2 *A* is the location of the anode, then the distance *A-B* perpendicular to the skin is the focal-skin distance *d*. At any other point along the curve *B-D*, which is concentric with the anode,

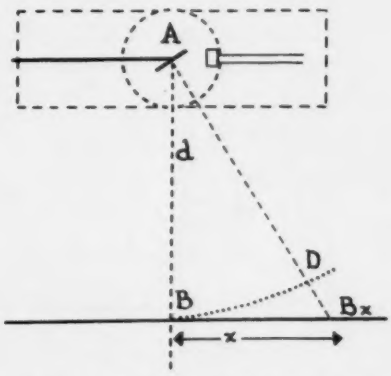

Fig. 2.—Illustration of the application of the inverse square law. The explanation is found in the text.

the intensity measured is the same as at *B*. But at any point B_x, x centimeters from *B* and in a plane perpendicular with the center beam *A-B*, the radiation intensity will be proportional to the square of the distance *d* divided by the sum of the squares of *d* and of *x*, i. e., $d^2 / (d^2 + x^2)$. This is the inverse square law of distance, and this law holds accurately when the (anode) target of the tubes is flat and the bulb of the tube is of uniform thickness and concentric with the focal spot.

Measurements were made with a shock-proof tube in a plane perpendicular with the central beam at several distances from the center *B*. The tube voltage was 52 kilovolts, 10 milliamperes, and there was no filter except the tube window, the oil layer and the window in the tube housing.

The procedure employed for obtaining the figures which proved the inequality of the fields of distribution of roentgen rays emitted by

shock-proof apparatus was as follows (fig. 3): A large piece of paper was ruled off at integral distances of 1 inch (2.5 cm.). Directly over the center of the paper and at an appropriate distance was placed the anode of the x-ray tube. The ionization chamber of the ionometer was placed on the center of the paper. A dose of 100 r was applied. The chamber was then moved an inch at a time from the center lengthwise with the tube axis, first toward the anode side and then away from the anode. Each time the chamber was moved, a reading was recorded.

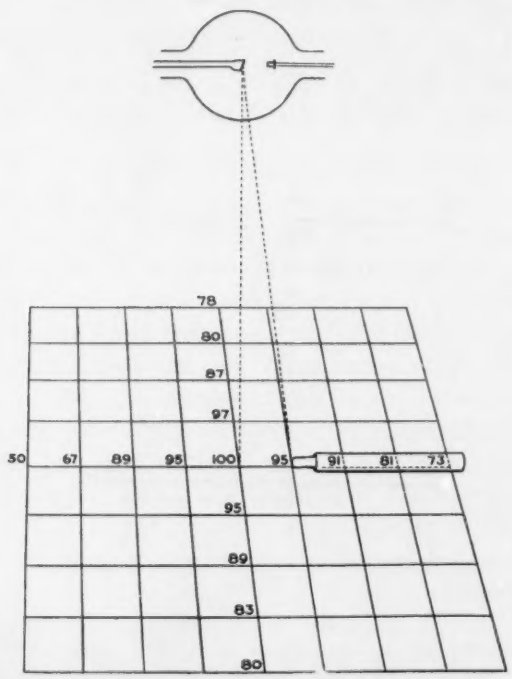

Fig. 3.—The method employed in measuring the inequality of the field of distribution of a roentgen-ray beam emitted by shock-proof apparatus.

The experiment was continued and measurements were recorded crosswise to the tube axis. The results are indicated as follows (these figures are plotted in fig. 5 as curve *A*):

				78				
				80				
				87				
Anode				97				
50	67	89	95	100	95	91	81	73
				95				
				89				
				83				
				80				

The measured values show that there is an appreciable decrease in the region of the anode. This falling off of intensity is known to be caused by interference of the heel of the anode. The heel effect is not the only cause for the decrease in intensity. The greater thickness of the oil through which the peripheral rays have to pass also accounts for the lowered intensity.

If the heel effect and the oil effect are eliminated and rays emitted from a point source and obeying the inverse square law are considered, the measurements made lengthwise with the tube axis should be as follows (these figures are plotted in fig. 5 as curve *B*):

Anode				Center				
92.8	95.7	98	99.3	100	99.3	98	95.7	92.8

In the next experiment measurements were made with rays passing through the glass of the tube, the oil layer and the window of the tube housing at equal distances from the focal spot. If no abnormal conditions exist, the measured values should be the same as those already given. However, different values were obtained and these are indicated as follows (these figures are plotted in fig. 5 as curve *C*):

					26.5 90.0 92.5 94.5 97.3					
Anode										
26	80	91	95	97	100	97	93	89	82	73
					97.5 95 93 89 27					

These measurements instead of giving the same results at all points reveal a deviation from the expected results, and the deviation of these results is different in the length axis and in the crosswise axis of the tube. The intensity drops off from the center toward the borders of the irradiated field. The decrease so found plus the decrease due to the inverse square law for measurements in a plane should substantially equal the results measured in a plane, if it is to confirm the deduction that the abnormal field decrease toward the border is due to a cause inherent in the tube.

The layer of oil through which the rays have to pass is either of uniform thickness and flat or thicker at the borders than in the center. The shape of the layer of oil is dependent on the window of the x-ray tube and that of the housing as well as on the location of the x-ray tube in the housing. The layer of oil through which roentgen rays pass

affects the field of distribution. To confirm this view experiments were made with an x-ray tube having walls of uniform thickness and concentrically curved about the focal spot, i. e., a universal Coolidge type tube. A container cap of cardboard was rendered waterproof and filled with transformer oil, and the tube was lowered to touch the brim of the cap. This produces a condition which exists when the outer window in the housing is flat and thus the oil layer is less thick in the center as compared with the borders, as is illustrated in figure 4. The following measurements were made in a plane, similar to those described in the preceding parts (measurements made lengthwise to the tube axis):

Anode				Center				
75	86	94	98	100	97	93	84	74

The results are plotted in figure 5 as curve *D* and indicate a decrease of radiation intensity from the center out toward the brim of the field

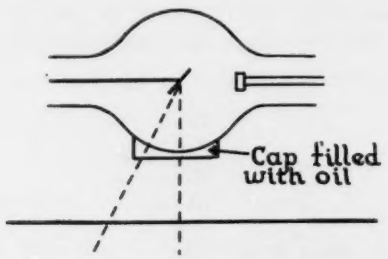

Fig. 4.—Diagram showing roentgen rays emanating from universal Coolidge tube and passing through a cap filled with oil. The rays at the periphery pass through a thicker layer of oil than those in the center.

similar to that obtained with the shock-proof oil-immersed type of x-ray tube.

These measurements indicate a condition in the combination of tube, insulating oil and tube housing window which causes an abnormal decrease of the radiation intensity from the center out toward the border of the field. This decrease, not being based on uniform factors, is naturally not uniform with all oil-immersed tubes and would have to be determined experimentally for every tube. This would cause complications and difficulties in computing the field when overlapping areas are applied to irradiated large areas. Therefore, it is suggested that windows of oil-immersed tubes, the oil layer and the window in the housing be constructed so as to conform with the conditions outlined, under which the inverse square law will hold substantially accurately. This concretely means that the window in the tube housing should be concentric with oil-immersed tubes so that the thickness of oil is uniform

in all directions. Also that oil-immersed tubes should contain targets at an angle of 45 degrees with round focus, as in universal Coolidge tubes.

The data of measurements previously reported are plotted in figure 5. It is observed from the curves obtained that a similar deviation from the inverse square values is obtained with the shock-proof tube as well as with a non-shock-proof tube with an added oil chamber.

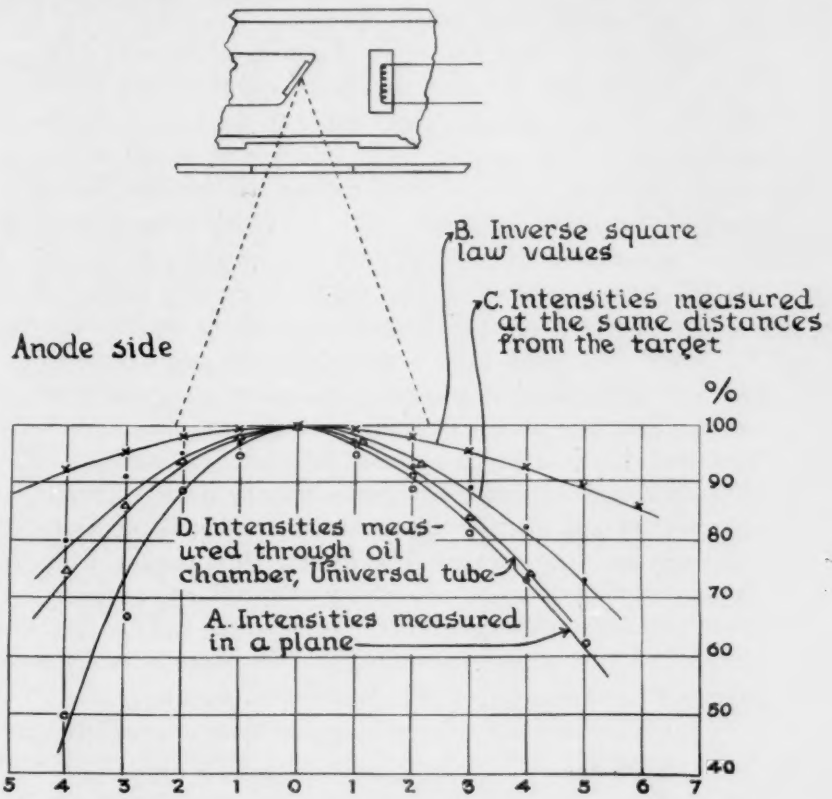

Fig. 5.—Curves *A, B, C* and *D*, representing the falling off of intensity at the periphery under varying conditions, are plotted so that they can be easily compared.

PRACTICAL ADVANTAGES OF SHOCK-PROOF APPARATUS

At first it was thought that shock-proof apparatus was cumbersome, difficult to manipulate and unsatisfactory for treating cutaneous lesions. Experience, however, has shown that shock-proof apparatus is even more flexible in clinical use than many of the unprotected machines. It is possible to irradiate safely areas which are difficult to approach. Such places may be reached with considerably greater ease

and with the expenditure of less time. The perineum, the perianal area, the vulva, the axillas and the anterior surface of the neck are difficult to irradiate at short distances, but with the shock-proof apparatus it is possible to get the x-ray tube in the exact position without the necessity of the patient's assuming unusual positions and without use of cumbersome protection. Such areas are treated entirely without danger of electrical shock and with far greater protection from scattered and secondary radiation. This means a saving of time, greater comfort to the patient and of course greater safety.

Practical experience has shown that even infants with angiomas can have lesions treated with this shock-proof apparatus with perfect control of all factors and without danger either to the baby or to the parents holding the baby in position. The tube can be placed so close to the lesions that only a few seconds' exposure is required to deliver the required quantity of radiation. This is possible because the apparatus is free of danger from electrical shock and the radiation is confined to a selected opening. Electrical factors can be changed easily and quickly so that lesions regardless of the type and position can be irradiated with the appropriate quality and quantity of radiation. This is especially true in treating small areas, such as malignant cutaneous lesions, where a cauterizing dose of soft radiation (50 kilovolts) may have the advantage over a more penetrating type of radiation (120 kilovolts and 3 mm. of aluminum). This of course means that the so-called contact therapy can be closely simulated without having the special apparatus that is ordinarily used for this type of treatment. It is possible with this type of apparatus, therefore, to utilize very soft unfiltered roentgen rays (50 kilovolts) and radiations of moderate hardness (120 to 140 kilovolts and 3 to 6 mm. of aluminum filter). This range is sufficient for the roentgen treatment of all types of cutaneous lesions.

Because of the safety of handling this apparatus and the ease with which the factors may be changed, the advantages enumerated may turn out to be disadvantages. Carelessness and disregard of the rules of safety may lead to danger both to the patient and to the operator. In using this safer apparatus one has to be even more careful than when using unprotected x-ray generators.

Ginsberg and Landauer,[5] discussing this general subject, stressed the unevenness of the field of radiation of flat surfaces with modern shock-proof apparatus. Their findings are essentially the same as ours. However, we wish to disagree on the remedies suggested. The derma-

5. Ginsberg, J. E., and Landauer, R. S.: Dermatologic Aspects of Roentgen Ray Field Distribution, Arch. Dermat. & Syph. **45**:364 (Feb.) 1942.

tologists have been using for years the principle of overlapping in treating large areas. We believe that this technic should be retained for the following reasons:

1. Shifting technic may lead to errors causing irreparable damage to tissues.

2. The necessity of charting the field of each apparatus is confusing and expensive and may lead to errors.

3. The structural changes suggested in our article are simple and feasible, avoid charting of the field of each apparatus and make unnecessary the shifting of present and time-tried methods of treating large areas.

SUMMARY AND CONCLUSIONS

Shock-proof and x-ray-proof apparatus are commonly used by dermatologists.

The advantage of safety and greater flexibility makes this type of apparatus of greater usefulness to dermatologists.

The quality of radiation corresponds to that of the older apparatus, which is not shock-proof. The number of roentgens required to produce erythema for different qualities of radiation are given.

The field of distribution is not uniform, and therefore the principle of overlapping in treating large areas cannot be applied. Suggestions are made to overcome this serious defect.

Practical advantages of shock-proof apparatus are discussed.

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ABSTRACT OF DISCUSSION

DR. C. GUY LANE, Boston: The authors have emphasized the three salient features of shock-proof apparatus: first that it is shock proof; second, that it contains a small oil-immersed tube, and, third, that the angle of the target is 20 to 30 degrees instead of 45 degrees. I think they also give the impression that the thin-walled Coolidge tube, which many dermatologists have used in the past and some still do use, has a half value layer of 0.26 mm., as compared with the half value layer of 0.8 mm. of the more modern apparatus with the thin-walled oil immersed tube.

This apparatus has numerous advantages in the matter of adaptability, flexibility and safety, of course, but the authors have done well to point out certain limitations in its use. When I began using this newer apparatus I was concerned, and still am for that matter, with the irradiation of large areas and the overlapping, or the lack of the ability to overlap perhaps, with the effect of filtration of the oil and also with the size of the port as well as the angle of the target. The size of the port, even if a 24 inch (60 cm.) or greater target-skin distance is used still makes accurate overlapping almost impossible, it seems to me.

With regard to filtration, the earlier work of Dr. Cipollaro has shown that filtration is not necessary, the unfiltered radiation being perfectly satisfactory for at

least the first 2 or 3 mm. of skin. My experience is interesting in this connection. Several months after my using the shock-proof apparatus and apparently standardizing radiation sufficiently well so that I was getting a good epilation, a patient appeared two or three weeks after irradiation with a very sharp line of alopecia across the top of the scalp. In other words, on one side there was good epilation and on the other side none. That was the first demonstration to me of the so-called heel effect. When I came to check up on the machine after making a photograph of the field, I found there was a flat side to the oval. In other words, the field of exposure, as represented on the roentgenogram, had a definite flat side, and an examination of the length of the field, that is, the long axis of the tube, showed what Dr. Cipollaro has already shown so well. In other words, on the anode side there was a very sharp falling off in the number of roentgens delivered, as compared with the points farther away.

I agree with the recommendations which the authors have made with regard to the curved surface of the housing of the tube and the 45 degree angle, and I have also wondered whether a square port and a larger port would make the apparatus more adaptable for dermatologic use.

Dr. George C. Andrews, New York: The amount of protection given by the shock-proof cables varies considerably according to the age of the cables. Shock-proof cables prevent electric shocks, but when the cables age there may be a breakdown of the insulation, resulting in an arcing between the center conductor and the outside grounded shielding. If the exposure is not immediately terminated and the patient happens to be in contact with the shielding at the point of breakdown, the patient may be badly burned whether grounded or not. It is therefore not advisable to have the cables in actual contact with the patients. In the large hospitals the cables wear somewhat over a year.

With the old type of equipment there have been a few accidents, mostly due to faulty installation. In an instance I heard about the high voltage wires were close to a radiator at the foot of the table, and there was a short circuit with a serious accident. However, in twenty years' experience I have not had any serious electrical accident with x-ray machines, and I doubt that many dermatologists have had. With ordinary care the non-shock-proof type of equipment has proved generally to be safe. I make that statement because there was some talk in New York state of having a bill introduced in the legislature to require all therapeutists to install new shock-proof machines. Shock-proof machines are not necessary for general safety. Even with them care must be taken.

Dr. Cipollaro has stated that the average angle of the tube anode is between 20 and 35 degrees. That applies to the Machlett tube and perhaps to others, but the General Electric shock-proof tube has the anode at an angle of 45 degrees. The only criticism I have of Dr. Cipollaro's paper is that he has experimented with his own machines, and one is likely to interpret from it that his results apply to one's own machine, which, of course, they don't. So general conclusions should not be drawn too freely from the work.

Treatment by overlapping is generally more accurate with the old type of apparatus than with the shock-proof apparatus. As to the tube housing, as a matter of fact, the amount of protection given by the tube housing varies greatly in shock-proof machines of different makes. It should, of course, be realized that even with the best protected tube, it is still necessary to protect against primary radiation passing through the aperture and against secondary rays scattered from the patient. The matter of tube housing is very important and has a bearing on this problem that Dr. Cipollaro has mentioned of the distribution of the different intensities of radiation throughout the field and affects it, I think, even more importantly than the oil through which the radiation passes.

I should be interested to know whether the erythema dose with the 0.26 mm. half value layer radiation was 300 r. I do not imagine it was, and I imagine that Dr. Cipollaro in referring to that soft thin-walled tube meant a tube that is really out of date and not in use any more. I know that he for years has

propounded a 300 r erythema dose, and I imagine it was with the 0.8 mm. of aluminum quality of radiation and not with 0.26 mm. of aluminum. Of course there will be a great difference in the erythema dose with these two qualities of radiation.

In my clinic a Machlett tube is used, unfiltered, with the shock-proof apparatus at 100 kilovolts, and the half value layer is 0.8 mm. of aluminum. Other makes of shock-proof tubes, however, with this voltage of unfiltered radiation have a radiation quality as high as 1.5 mm. of aluminum. Thus it is not possible with experiments with one machine to make a general statement regarding the number of roentgens per erythema dose. In the Vanderbilt Clinic for years, since Braestrup and I published a paper showing that radiation at 50 or 60 kilovolts filtered through 2 mm. of aluminum has a greater absorption in the first centimeter of skin than the other old types of radiation, such as 100 kilovolts unfiltered, I have routinely used 60 kilovolts through 2 mm. of aluminum at 20 milliamperes, and the output is measured as a half value layer of 2.0 mm. of aluminum.

One can obtain quite a difference in ray quality with different types of apparatus at the same voltages and corresponding differences in the number of roentgens per erythema dose.

It is physically impossible, as long as the aperture of the tube housing is close to the anode, to get a distribution of the emerging beam conforming to the inverse square law. This is because a portion of the field, which might be called the umbra, gets radiation from the entire surface of the anode, whereas the edges of the field, called the penumbra, get radiation from only a part of the surface of the anode.

When one considers the oval shape of the anode and the side effects as well as the effects along the long axis, one can see that there is a great variation in the peripheral radiation. As long as the tube housing is built with an aperture close to the anode, one is bound to get this penumbra effect, which will have a very great influence on the intensity throughout the radiation field.

DR. MARION B. SULZBERGER, New York: If one takes the arc of the tube and the flat surface of the window, then, as Dr. Cipollaro has pointed out, one gets a thicker layer of oil at the periphery of the window than at the center. The two surfaces diverge, that is, the arc of the tube curves up and the window is approximately flat, so that there is a thicker meniscus at the periphery than at the center. One effect of this increased thickness of oil must be a decrease in the amount of radiation at the edges of the field. That is one of the important fectors. There must also be a greater filtration at the edges of the field than at the center, and the quality of the rays at the edges of the field must be slightly different from that of the central rays. They must be slightly harder at the periphery than at the center.

Another point is that the surfaces irradiated in dermatologic practice not only are not the ideal concave surfaces with all points equidistant from the focus of the tube but as a rule are not even flat surfaces. They are usually convex surfaces, for instance, a head, a face or a breast, so that the fact of error of the periphery due to increase with the square of the distance causes a significant diminution of dose at the edge of the field.

However, I believe that while all of these matters are interesting, they are not as important for dermatologic work as they might appear to be, because there are still so many other so-called secondary factors of error which enter into practical irradiation therapy. For ordinary work, for instance, the back scatter and the size of the field irradiated are perhaps much more important than any other secondary factors. An "erythema dose" on an area 1 cm. in diameter may be more than five to ten or more times as much as an erythema dose on an area which is 10 to 20 cm. in diameter. This variation is so great that it is often more important than the minor variations due to apparatus and distance which are discussed in the authors' paper.

I have been using shock-proof apparatus now for ten years, and I have continually tried to get manufacturers to make tubes designed exclusively for the purpose of dermatologic therapy. The tube that I am using I believe is still one primarily designed for roentgen diagnosis. If Drs. MacKee, Cipollaro and Mutscheller can succeed where I have failed and get tubes made specially for dermatologic roentgen therapy, one can of course modify the angulation and the position of the anticathode to produce improvement and obviate the cutting off of the bundle of rays by the anticathode "shadow." Also, one might be able to make a much cheaper apparatus. The ideal radiation for dermatologic superficial therapy should be absorbed within the first millimeter or so of the skin and does not need to—and indeed should not—go in any deeper; 30 to 40 kilovolts should be sufficient for this radiation. With the 60, 70, 80 and 100 kilovolts now being used, most of the rays are pressed past the area of the skin where one would like to have them absorbed in superficial therapy. If my understanding is correct, x-ray tubes can be manufactured which are optional for superficial therapy, will run at about 30 to 40 kilovolts, will effect considerable savings of cost and essential materials, will be safer even than the present models and probably could be plugged in any ordinary alternating light socket.

DR. ARTHUR MUTSCHELLER, New York: In the discussions it has been said that the angle of tilt of the anode has been changed. The angle was changed from 45 degrees to a lesser tilt because of the introduction of the so-called line focus used for roentgenographic work, but the line focus has no advantage for therapeutic tubes. The round focus tube, as Dr. Andrews has pointed out, does not give rise to the formation of penumbras, and this is a further argument in favor of the round focus.

With regard to the filtering value of the oil, there is a fundamental principle that a substance in order to be a useful homogenizing filter must be of a heavier atomic weight than the substance to be penetrated; therefore, oil which has substantially the same composition as tissue—it is organic material—does not filter very much; nevertheless, it does reduce the total radiation intensity, that is, it wastes radiation.

DR. ANTHONY C. CIPOLLARO, New York: The question of the opening in the tube housing has already been discussed. If the target is near to the opening or if the skin-target distance is increased, the field of irradiation will be large. The two important factors that affect the field of irradiation are the angulation of the target and the unevenness of the layer of oil between the tube and its housing. Dr. Mutscheller has already emphasized that most shock-proof tubes have a line focus. For routine dermatologic irradiation a round focus tube is more desirable.

I agree with Dr. Anderson in regard to negligence and accidents occurring during the operation of x-ray machines. I should also like to state that I do not know of a single instance of death following electric shock from the use of a dermatologic unit, even with the old-fashioned, unprotected apparatus.

Our experiments have shown that there is no essential difference in the quality of radiation emitted by modern shock-proof apparatus and by unprotected x-ray apparatus. Therefore no change in technic is required when one is using shock-proof apparatus.

The erythema dose is variable, depending on radiation quality or on filtration and voltage. A higher number of roentgens are required to produce erythema when highly filtered and high voltage roentgen rays are employed. For soft radiation a smaller number of roentgens are required to produce an erythema. Basing our conclusion on hundreds of clinical tests, Dr. MacKee and I believe that 300 r is an average dose for an erythema with nonfiltered low voltage roentgen rays. This quantity of radiation is also the epilation dose (MacKee, G. M., and Cipollaro, A. C.: The Roentgen Unit in Dermatology, ARCH. DERMAT. & SYPH. **30**:761 [Dec.] 1934; Roentgen Dosage in Dermatology Expressed in International Roentgens, ibid. **41**:1-7 [Jan.] 1940).

Dr. Andrews is laboring under a misconception if he thinks that all the data contained in this paper and those which formed the basis for our conclusions were based on a single or a small series of experiments with a single machine. It is a matter of record that to obtain these data it required the combined talents of two clinicians especially interested in the physics and mechanics of x-ray apparatus and a physicist. At least twenty x-ray machines were used in our experiments, hundreds of cutaneous tests and epilation tests were performed and the time expended has been about ten years. Experiments are still going on.

Dr. Sulzberger brought out a very interesting point. In a previous communication (Cipollaro, A. C., and Mutscheller, A.: Absorption of Roentgen Rays by the Skin: Experimental Determinations, ARCH. DERMAT. & SYPH. **41**:87 [Jan.] 1940) it was stated that 50 kilovolt radiation is about as adequate as 100 kilovolt radiation in the treatment of cutaneous diseases. Now if one can obtain machines that have a maximum kilovoltage of about 60, that type of apparatus can be manufactured at a lower cost.

SARCOIDOSIS

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HISTORY

Jonathan Hutchinson [1] in 1875 recorded what was probably the first clinical description of sarcoidosis; his patient had purplish nodular sharply circumscribed lesions on the fingers, forearms and legs, together with nontender swelling of one finger. Besnier [2] in 1889 described a symptom complex consisting of nodular reddish blue lesions of the face and nose in conjunction with swellings of the fingers and gave it the name of lupus pernio. In 1897 and 1899 Boeck [3] reported the first of his cases of "multiple benign sarcoid," considering this disease allied to the sarcoma group and confined to the skin. He later changed the name to benign miliary lupoid, when he recognized the resemblance of this condition to tuberculous processes.

In 1902 Kienboeck described the cystic osseous changes of the fingers and toes found on roentgen examination, and Kreibich [4] in 1904 first associated these with the cutaneous changes of lupus pernio. It was not until 1915, when Kutznitzky and Bittorf [5] first observed the characteristic pulmonary changes that the widespread nature of sarcoidosis was recognized. However, it was Schaumann who integrated and correlated all these varied clinical manifestations as a single systemic disease.

Read before the Section on Dermatology and Syphilology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

From the departments of Dermatology and Syphilology of the University of Pennsylvania and of the Woman's Medical College of Pennsylvania and the Philadelphia General Hospital.

The clinical material reported in this paper forms part of the thesis submitted to the faculty of the Graduate School of Medicine of the University of Pennsylvania, in partial fulfilment of the requirements for the degree of Doctor of Medical Science (D.Sc. [Med.]) for graduate work in dermatology and syphilology.

1. Hutchinson, J.: Illustrations of Clinical Surgery, London, J. & A. Churchill, 1875, p. 42.

2. Besnier, E.: Lupus pernio de la face, Ann. de dermat. et syph. **10**:333, 1889.

3. Boeck, C.: Multiple Benign Sarcoid of the Skin, J. Cutan. & Genito-Urin. Dis. **17**:543, 1899.

4. Kreibich, K.: Ueber Lupus pernio, Arch. f. Dermat. u. Syph. **71**:3, 1904.

5. Kutznitzky, E., and Bittorf, A.: Boeck'sches Sarkoid mit Beteiligung innerer Organe, München. med. Wchnschr. **62**:1349, 1915.

He conclusively demonstrated that all the apparently different clinical entities aforementioned are but part of a systemic, characteristic and identical tissue reaction. In 1936 he summarized his researches and experiences of the preceding twenty years in a classic review of the subject.[6] With 4 autopsies and exhaustive animal studies he proved once more that lupus pernio as well as the cystic osseous lesions studied by Jüngling[7] in 1919 and named osteitis tuberculosa cystoides and the epithelioid tubercles found disseminated throughout lymph nodes, lungs and spleen were all part of the same syndrome. Because of its clinical resemblance to Hodgkin's disease, he gave it the name lymphogranulomatosis benigna.

This clinical entity, variously named Besnier-Boeck-Schaumann disease, sarcoidosis, benign lymphogranulomatosis and noncaseating tuberculosis, has received considerable attention in the dermatologic literature, both in this country and abroad. Among outstanding contributions may be mentioned the monograph of Kissmeyer,[8] published in 1932, and that of Pautrier,[9] which appeared in 1940. Internists in this country have become interested in this subject in relatively recent years, and admirable surveys have been contributed by such men as Longcope and Pierson[10a] and Pinner[11] among others.

CLINICAL CHARACTERISTICS

The basic pathologic lesion of sarcoidosis, whether it is localized in the skin, the lymph nodes, the spleen, the lungs, the bone marrow or the salivary or lacrimal glands, is the so-called "hard" tubercle, a circumscribed collection of epithelioid cells with a sparse admixture of Langhans type giant cells and a striking scarcity or even absence of lymphocytic tissue response. Central necrosis and caseation are almost never found (figs. 1 and 2).

The whole disease process consists of a more or less widespread infiltration of all the structures comprising the reticuloendothelial system. For this reason Pautrier[9] preferred the designation reticulo-

6. Schaumann, J.: Lymphogranulomatosis Benigna in the Light of Prolonged Clinical Observations and Autopsy Findings, Brit. J. Dermat. **48**:399, 1936.

7. Jüngling, O.: Ueber Osteitis tuberculosa multiplex cystica, Fortschr. a. d. Geb. d. Röntgenstrahlen **27**:375, 1919.

8. Kissmeyer, A.: La maladie de Boeck, Paris, Masson & Cie, 1932.

9. Pautrier, L. M.: La maladie de Besnier-Boeck-Schaumann, Paris, Masson & Cie, 1940.

10. (*a*) Longcope, W. T., and Pierson, J. W.: Bull. Johns Hopkins Hosp. **60**:223, 1937. (*b*) Longcope, W. T.: Sarcoidosis, or Besnier-Boeck-Schaumann, Disease, J. A. M. A. **117**:1321 (Oct. 18) 1941.

11. Pinner, M.: Noncaseating Tuberculosis: An Analysis of the Literature, Am. Rev. Tuberc. **37**:690, 1938.

12. Footnote deleted on proof.

endotheliosis for this syndrome. The course is usually slowly progressive and only rarely leads to death. Most reported fatalities were due to displacement of sufficient vital tissue, such as myocardium or bone marrow, so as to be incompatible with life, or to the more rare development of tuberculosis. In our group of 15 patients 3 died, 1

Fig. 1.—Section of an epitrochlear lymph node (hematoxylin and eosin; × 92). Nodular aggregates of epithelioid cells have largely displaced the lymphoid tissue elements.

of pulmonary tuberculosis developing within a year of the first appearance of sarcoid lesions, 1 of a massive pulmonary infarction caused by pressure from tremendously enlarged mediastinal lymph nodes and the third after a slow course, of four years, of widespread amyloidosis. The remaining 12 patients are all living. Five of these have spon-

taneously recovered, or, at least, all detectable lesions have undergone involution (2 white persons and 3 Negroes). The disease in the remaining 7 is slowly progressing, periodic exacerbations developing with increase in number and size of lesions, followed by remissions, while the general state of health remains fairly good. All have been

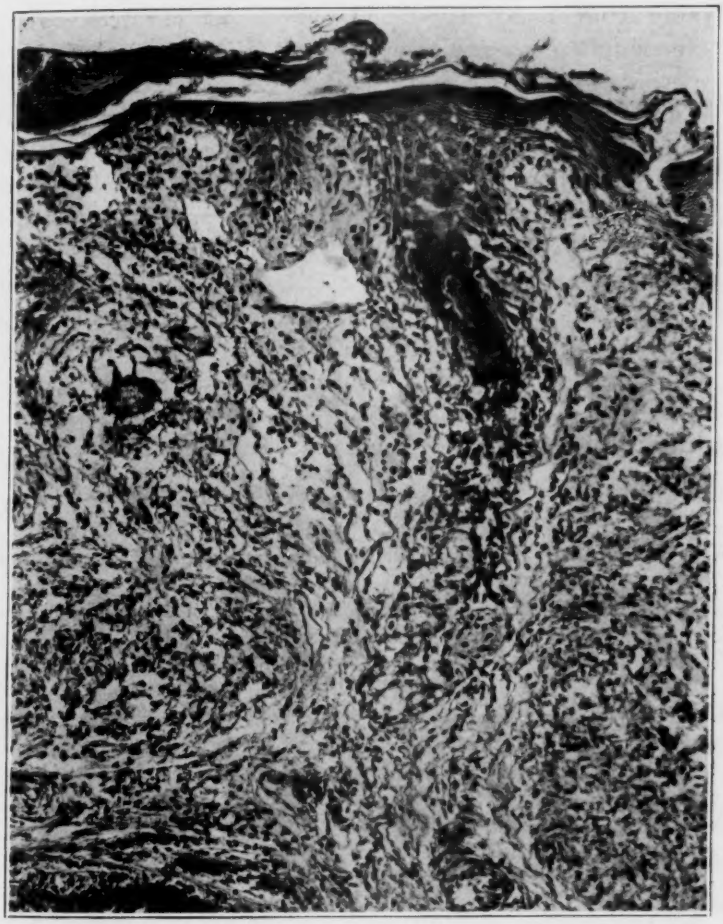

Fig. 2.—Section from a lesion on the scalp of the patient in figure 4 (hematoxylin and eosin; × 180). Endothelioid cell masses are surrounding a hair follicle and have produced thinning of the epidermis. A single Langhans giant cell is shown.

under clinical observation for more than one year, some for as long as six years.

PATHOGENESIS

Although the histologic appearance of sarcoidosis is clearcut, the cause remains a puzzle. Tubercle bacilli have been found in sarcoid

lesions by Kyrle,[13] Wende,[14] Dittrich,[15] Ruete [16] and Hudelo, Montlaur and Leforestier.[17] Frazier and Hu [18] demonstrated Spirochaeta pallida in a sarcoid-like lesion. Sarcoid-like leprosy has been frequently reported (Pautrier,[18a] Motta,[19] Filho [20] and Sáenz and Palomino [21]). The role of syphilis has been repeatedly stressed, especially by French investigators. Gougerot and Darier likewise pointed out that foreign bodies may act as etiologic agents in the production of sarcoid. A virus has been postulated by numerous authors (Kissmeyer), but the supportive evidence is also not conclusive. Lesions identical with those of sarcoid disease have been produced experimentally by the injection of the phosphatide (lipid) fraction of the tubercle bacillus by Sabin [22] and her associates, who showed that this fraction provokes a tissue response identical with that of the "hard" or "proliferative" tubercle. There results a proliferation of monocytes which engulf the lipids and so become endothelioid cells. These cells may later fuse, producing typical multinucleated giant cells. Sarcoid-like lesions have also been produced by the injection of bovine tubercle bacilli of low virulence into rabbits and guinea pigs (Smithburn [23]) and of virulent tubercle bacilli into rats (W. Jadassohn [24]). Although the actual isolation of tubercle bacilli by culture or animal inoculation has been only rarely

13. Kyrle, J.: Die Anfangsstadien des Boeckschen Sarkoids: Beitrag zur Frage der Ätiologie dieser Dermatose, Arch. f. Dermat. u. Syph. **131**:33, 1921.

14. Wende, G.: Nodular Tuberculosis of the Hypoderm, J. Cutan. Dis. **29**:1, 1911.

15. Dittrich, O.: Ueber den direkten Tuberkelbazillen Nachweis beim Lupus pernio und beim Sarkoid Boeck, Dermat. Ztschr. **60**:395, 1931.

16. Ruete, A.: Zur Aetiologie der Boeckschen Erkrankung, Dermat. Ztschr. **37**:129, 1922.

17. Hudelo; Montlaur, and Leforestier: Lymphogranulomatose de Schaumann (lupus pernio) à forme anormale, Bull. Soc. franç. de dermat et syph. **32**:109, 1925.

18. Frazier, C. N., and Hu, C. K.: Isolation of Treponema Pallidum from Subcutaneous Sarcoid, Proc. Soc. Exper. Biol. & Med. **30**:898, 1933.

18a. Pautrier, L. M.: Leprome à histologie de sarcoide dermique, Bull. Soc. franç. de dermat. et syph. **41**:1284, 1934.

19. Motta, J.: Les sarcoides de la lepre, Ann. de dermat. et syph. **2**:1180, 1931.

20. Filho, R.: Etiology of Besnier-Boeck's Disease, Foreign Letters, J. A. M. A. **105**:1205 (Oct. 12) 1935.

21. Sáenz, B., and Palomino, J. C.: Tuberculoid Leprosy, Arch. Dermat. & Syph. **39**:456 (March) 1939.

22. Sabin, F. R.: Cellular Reactions to Tuberculo-Proteins Compared with Reactions to Tuberculo-Lipids, J. Exper. Med. **68**:837, 1938. Smithburn, K. C., and Sabin, F. R.: Reactions of Normal and Tuberculous Animals to Tuberculo-Protein and Tuberculo-Phosphatide, ibid. **68**:641, 1938.

23. Smithburn, K. C.: Virulence of Bovine Tubercle Bacilli, Am. Rev. Tuberc. **36**:637, 1937; Histopathology of Experimental Tuberculosis, ibid. **36**:659, 1937.

24. Jadassohn, W.: L'origine tuberculeuse de la maladie de Boeck, Bull. Soc. franç. de dermat. et syph. **41**:1344, 1934.

accomplished with sarcoidosis, there is a mass of circumstantial evidence which tends to incriminate this organism as a factor in a majority of cases.

J. Jadassohn first advanced the concept of positive anergy to explain the unusual frequency with which absence of reaction to tuberculin occurs in sarcoidosis and the apparent mutual exclusiveness of "classic tuberculosis" and sarcoidosis. The finding by Pickert and Löwenstein [25] and W. Jadassohn and Martenstein [26] of tuberculin-neutralizing substances (anticutins) has not been corroborated in many instances of sarcoidosis reported in this country and could not be demonstrated in any of the 4 anergic patients who were so investigated in this series. Nevertheless, the theory that sarcoidosis represents a reaction of immunity to the tubercle bacillus or its products is an attractive one and has found some additional support in the more recent work on changes in serum proteins observed during the active stages of the disease. Salvesen [27] in 1935 was probably the first to note the decided increase in serum globulin and relative decrease in serum albumin, a finding common to disease processes involving the reticuloendothelial system. His work has been repeatedly confirmed, notably by Bing [28] and by Harrell and Fisher.[29] Seibert [30] has shown by electrophoretic methods that the globulin fraction accounting for this increase is chiefly gamma globulin, a rise in which apparently indicates some degree of resistance to tuberculous infection.

Parallel with this finding is the common occurrence of monocytosis in the differential blood count. Schaumann called attention to this, and we have found it to be fairly constant whenever clinical activity of the sarcoid lesions was manifest. Thus, of 13 patients examined during periods of clinical activity, monocyte counts of from 8 to 18 per cent were found in 7 and from 2 to 5 per cent in 6, frequently associated with a relative leukopenia (from 2,800 to 6,000 leukocytes).

In all of our cases a cutaneous biopsy was performed to confirm the diagnosis. Biopsy of lymph nodes, observations at autopsy and in 1

25. Pickert, M., and Löwenstein, E.: Eine neue Methode zur Prüfung der Tuberkulin Immunität, Deutsche med. Wchnschr. **34**:2262, 1908.

26. Jadassohn, W., and Martenstein, H.: Ueber die Abschwächung der Tuberkulinwirkung durch menschliches Serum, Klin. Wchnschr. **2**:1210, 1923.

27. Salvesen, H. A.: The Sarcoid of Boeck, Acta med. Scandinav. **86**:127, 1935.

28. Bing, J.: Further Investigations on Hyperglobulinemia, Acta med. Scandinav. **103**:545-565, 1940.

29. Harrell, G. T., and Fisher, S.: Blood Chemical Changes in Boeck's Sarcoid with Particular Reference to Protein, Calcium and Phosphatase Values, J. Clin. Investigation **18**:687, 1939.

30. Seibert, F. B., and Nelson, J. W.: Serum Proteins in Tuberculosis and Other Chronic Diseases as Demonstrated by Electrophoresis, Am. Rev. Tuberc., to be published.

instance removal of an enlarged lacrimal gland further corroborated the diagnosis. Cultures for tubercle bacilli and guinea pig inoculation were carried out in 6 instances with negative results.

Twelve of our 15 patients showed evidence of pulmonary involvement, chiefly changes due to enlarged mediastinal lymph nodes, increased pulmonary markings and in 2 instances diffuse marbling of the pulmonary fields (fig. 3). In 1 of the patients showing the last-mentioned changes fibroulcerative pulmonary tuberculosis developed, which ended fatally within a year. The tremendous hilar lymphadenopathy in 5 patients led to a presumptive diagnosis of Hodgkin's disease, and only when no response had occurred to roentgen therapy did further study establish the diagnosis of sarcoidosis. Many of the cases reported by Longcope [10b] and by Nickerson [32] followed a similar turn of events.

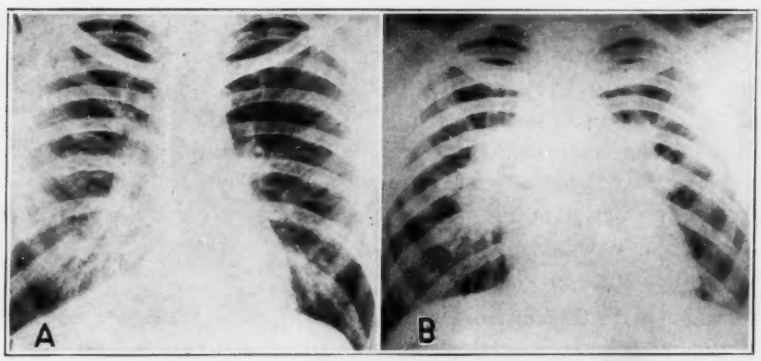

Fig. 3.—Two representative roentgenograms of the chest, *A* showing diffuse mottling of pulmonary fields and increased hilar shadows and *B* showing enlarged mediastinal lymph nodes, part of a generalized lymphadenopathy and splenomegaly.

Although the American Negro furnishes the bulk of the patients with sarcoid reported from the United States, the relative rarity with which fibrocystic osseous changes are recorded is striking. Twelve of our 15 patients had roentgen examinations of the small bones of the hands and feet, and in none could definite evidence of cystic change be found. One Negro patient who had repeated attacks of fusiform swelling of the fingers of both hands showed only questionable changes. This is in contrast to the reports from most European sources, in which fibrocystic changes seem to be common.

Recent observations have borne out Schaumann's contention that in practically all cases of sarcoidosis, if adequately studied, the disease will be found to be generally disseminated. Thus, sarcoid infiltrates

31. Footnote deleted on proof.

32. Nickerson, D. A.: Boeck's Sarcoid, Arch. Path. **24**:19 (July) 1937.

can be found in apparently normal tonsils, lymph nodes and bone marrow. It seems, therefore, futile to insist on strict clinical classification as to cutaneous and subcutaneous types (table 1).

In the dermatologic literature three chief morphologic variants of sarcoidosis have been distinguished:

1. Miliary lupoid, often associated with frank tuberculosis. This type of lesion is usually small and discrete and at times ulcerates. The disseminate follicular lupus of Tilbury Fox falls in this group.

2. Besnier-Boeck sarcoid, including lupus pernio and angiolupoid of Brocq and Pautrier, in which cutaneous involvement has been

TABLE 1.—*Involvement of Various Organs Found in Fifteen Patients with Sarcoidosis*

Organs Found Involved	No. of Patients	White (Total 3)	Negro (Total 12)
Skin	14	3	11
Lungs			
Hilar structures	11	3	8
Parenchyma	7	2	5
Lymph nodes	14	3	11
Spleen enlarged	7	2	5
Liver enlarged	6	2	4
Bones of the hands	1		1
Subcutaneous tissue	1		1
Eye			
Cornea	2		2
Uveal tract	2		2
Conjunctiva	2		2
Lacrimal gland	1		1
Mucous membranes			
Nasopharynx	2		2
Larynx	2		2
Urinary bladder	1		1

described as present alone or accompanied by lesions of any or all parts of the reticuloendothelial system (Schaumann's disease).

3. The subcutaneous sarcoid of Darier-Roussy, which manifests more deep-seated lesions and often merges clinically into erythema induratum (Bazin).

To these three groups must be added a fourth, the more recently described sarcoid type of tuberculosis of the American Negro. Klauder [33] in 1925 and Klauder and Weidman [34] in 1926 described the first case of this type, which began with a psoriasiform papular eruption and underwent involution with atrophic scarring, the patient ultimately

33. Klauder, J. V.: Multiple Sarcoid-Like Granulomas of the Skin of Undetermined Nature, Arch. Dermat. & Syph. **12**:171 (Aug.) 1925.

34. Klauder, J. V., and Weidman, F. D.: Multiple Sarcoid-Like Granulomas of the Skin of Undetermined Nature, Arch. Dermat. & Syph. **13**:675 (May) 1926.

dying of tuberculosis. Ketron and Ginsberg[35] reported 10 similar cases, and a number of excellent reviews have appeared in the American dermatologic literature (Crawford,[36] Nomland,[37] Jordon and Osborne[38] and Bloom and Mendelsohn,[39] to say nothing of numerous isolated case reports). Twelve cases of this type are included in this report. The consensus is that the condition is a tuberculosis of the skin of hematogenous origin, assuming sarcoid features due to unusual immunologic reaction on the part of the American Negro.

The cutaneous lesions observed in our series of 11 Negro patients were of five main types:

1. A superficial scaling, erythematous variety, healing with atrophic scarring. This type resembles lupus erythematosus and involves especially the scalp and face. On the surface of the lesions telangiectatic vessels can frequently be seen (fig. 4).

2. Grouped and scattered pinhead-sized to cherry-sized superficial nodules. These often develop from small psoriasiform papules but soon lose their scale. They are distributed particularly about the eyelids and inner canthi, the nose and the mouth, generally increasing in size and number rather slowly. Three of our patients experienced spontaneous remissions with disappearance of the lesions for two to three years, accompanied by an increase in reactivity to tuberculin, general improvement in health and a gain in weight (fig. 5).

3. Brownish red, flat, slightly indurated plaques of various sizes, assuming at times annular configurations with central atrophy. Brownish macules can at times be shown, by diascopic pressure, scattered throughout the lesion. This type of lesion may disappear entirely without residua or may leave atrophic scars resembling those of nodular-ulcerative syphilis (fig. 6).

4. Nodular-ulcerative lesions of the legs resembling in appearance and course those of erythema induratum (fig. 7).

5. In a single patient cherry-sized to walnut-sized subcutaneous nodules were present scattered over the back, chest and arms.

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35. Ketron, L. W., and Ginsberg, L.: Tuberculosis of the Skin in the Negro, Internat. Clin. **3**:118, 1936.

36. Crawford, S.: Cutaneous Nodulodiscoid Tuberculosis of Anergic Type with Development into Active Pulmonary Tuberculosis, Arch. Dermat. & Syph. **27**:766 (May) 1933.

37. Nomland, R.: Hematogenous Cutaneous Tuberculosis (Sarcoid) in Negroes, Arch. Dermat. & Syph. **30**:59 (July) 1934.

38. Jordon, J. W., and Osborne, E. D.: Besnier-Boeck's Disease, Arch. Dermat. & Syph. **35**:663 (April) 1937.

39. Bloom, D., and Mendelsohn, H. V.: Cutaneous Tuberculosis in the Negro: A Clinical Entity, Arch. Dermat. & Syph. **36**:937 (Nov.) 1937.

Fig. 4.—*A*, an erythematous scaling and atrophic sarcoid lesion of the scalp, resembling lupus erythematosus; nodular lesions of the eyelids, nose, chin and area anterior to the right ear. *B*, the same patient two years later. All lesions have spontaneously (?) disappeared, leaving an atrophic scar of the scalp.

Fig. 5.—*A*, small nodular sarcoid lesions of the eyelids with larger plaques on the forehead, nose and chin. *B*, disseminated soft smooth nodules of the back and arms. These lesions began three months before as psoriasiform papules.

TREATMENT

In spite of a thorough trial of most therapeutic agents mentioned in the literature, I am convinced that to date no satisfactory treatment exists. Four of our patients who also had syphilis were adequately treated with arsenicals and bismuth without benefit to the sarcoid lesions. In fact, 3 of these patients seemed to suffer exacerbations of

Fig. 6.—A patient with sarcoidosis of six years' duration, showing older large circinate lesions of the forearms and recently developed small nodules of the eyelids, lips and nose. This patient also has an active tuberculous uveokeratitis of the right eye.

their cutaneous lesions when antisyphilitic treatment was begun. Gold sodium thiosulfate, silver neoarsphenamine, tuberculin, chaulmoogra oil esters, diphtheria toxoid and peptone injection therapy was given to these patients without notable results. In 1 instance involution of lesions occurred following desensitization with an avian tuberculin, to which the patient was found to react. In 1 other case electrodesiccation

of the cutaneous lesions was apparently successful, no new ones appearing. Five patients underwent a probable spontaneous "cure" while under no treatment at all, being merely given a nutritious diet and a modified tuberculosis regimen. The condition of the remaining 3 patients is unchanged.

SUMMARY

Fifteen cases of sarcoid disease are reported with clinical observation extending over periods of from one to seven years. Three of the patients were white and 12 Negroes. There were 2 men and 13 women in the group. The age of onset of lesions varied from 15 to 49, with half of the patients having their initial attack before the age of 30.

The course of the disease is benign. Three patients died, 1 of pulmonary tuberculosis, which developed within a year of the onset of the sarcoid lesions but was preceded by a disappearance of all the cutaneous lesions. Another patient died two years after disappearance

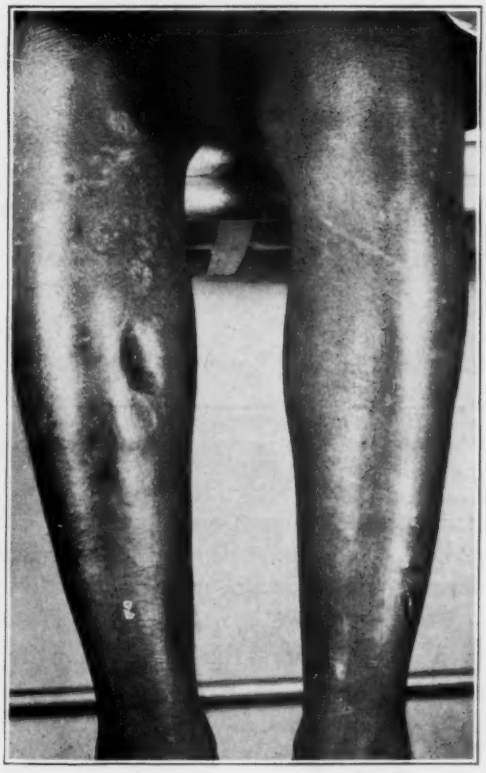

Fig. 7.—Scars and recent sarcoid lesions of the legs resembling erythema induratum.

of all the cutaneous lesions, the autopsy showing widespread amyloidosis. The third patient died within nine days of admission to the hospital of pulmonary infarction due to pressure from tremendously enlarged mediastinal lymph nodes. Five patients (2 white persons and 3 Negroes) underwent spontaneous recovery with disappearance of cutaneous changes, enlargement of the lymph nodes and improvement in general health. The condition of the remaining 7 patients was relatively unchanged; there were slight exacerbations and remissions.

Involvement in all cases was demonstrable in several organs, affecting the skin, lymph nodes, lungs, spleen and liver most frequently.

Tuberculin tests showed only 7 patients to be anergic; 7 reacted to 1 mg. or less of tuberculin (table 2).

TABLE 2.—*Tuberculin Reactivity of Fifteen Patients* with Sarcoidosis*

	Total Number of Patients	White	Negro	Stage of the Disease	
				Active	Inactive
No reaction to 10 mg.....	7	3	4	7	0
Reaction to					
1 mg.....	3	1	2	2	1 (white)
0.1 mg.....	2	..	2	2	..
0.01 mg.....	3	..	3	1	2

* Five patients were given tuberculin tests during periods of quiescence as well as during periods of clinical activity. One reacted to the same amount of tuberculin during both periods, and 2 did not react during clinical activity but did react during remission.

Anticutins could not be demonstrated in the serums of 4 anergic patients so examined. No clue as to causative organism could be obtained by bacteriologic methods and animal inoculation.

Three of the patients on whom determinations of serum protein were made showed decided increase in the globulin fraction.

The differential blood count revealed a monocytosis, with a count of from 8 to 18 per cent, in over half of the cases during active phases of the disease.

Treatment with a wide variety of agents was unproductive of noteworthy results.

SUMMARY AND CONCLUSIONS

Sarcoidosis is a systemic disease affecting all structures of the reticuloendothelial system and having a generally benign course.

Its relation to tuberculosis or other known disease entities remains obscure.

It is common in the American Negro, in whom the cutaneous lesions vary widely in clinical appearance, at times resembling lupus erythema-

tosus, psoriasis, lupus vulgaris and erythema induratum, but show the uniform histologic appearance of sarcoid.

Dr. Harold Israel, of the Henry Phipps Institute, and the staff of Dr. J. V. Klauder referred some of the patients. Dr. R. P. Custer, then pathologist to the Philadelphia General Hospital, gave permission to study the sections and autopsy records in the case. Dr. Herman Beerman gave help with photographs and histologic studies. Dr. John H. Stokes and Dr. Fred D. Weidman gave helpful criticism.

Dr. Phyllis Bott, Department of Chemistry, Woman's Medical College of Pennsylvania, carried out the serum protein determinations.

1930 Chestnut Street.

ABSTRACT OF DISCUSSION

Dr. Cleveland J. White, Chicago: This excellent study of 15 cases of sarcoidosis is a review of the type of syndrome originally described by Jonathan Hutchinson in 1875, studied again in detail by Besnier and Boeck and described in the epochal résumé of the extensive studies published by Schaumann in 1936. While tuberculosis looms as a strong possible etiologic factor, absolute proof is lacking, although Dr. Thomas found convincing evidence in half of her cases. Her findings reemphasized Schaumann's dictums that in practically all cases of sarcoidosis the disease is generally disseminated. Dr. Thomas pointed out the futility of strict clinical classification as to cutaneous and subcutaneous types. Dr. Thomas' observation of a monocytosis in most of her cases points out the possible valuable diagnostic aid of a histologic study. I wonder if Dr. Thomas found lesions of all the five types described in most of her Negro patients, as I have found some of each in a white man of 55 whom I am now studying. As to treatment, in a patient studied by Jelsamine at the Illinois Eye and Ear Infirmary, a generalized cutaneous sarcoidosis occurred subsequent to injections of tuberculin for a tuberculous keratitis. This may have been just incidental. Dr. Thomas' presentation is most timely and instructive.

Dr. George T. Harrell, Winston-Salem, N. C.: I have followed the study of sarcoidosis from the standpoint of the internist. As others have found, studies on the causation gave no clue. The negative findings suggested that there might be some unusual response on the part of the host to tubercle bacilli and perhaps other organisms. The presence of increased globulin fractions of blood protein suggests an unusual antibody; Dr. Thomas found that this is not an anticutin. In North Carolina a sample of purified protein derivative of avian tubercle bacilli furnished by Dr. Florence Seibert failed to elicit a reaction in concentration of 0.005 mg. It should be emphasized again, as Dr. Thomas has done, that sarcoid is really a generalized disease. I should like to know whether, in addition to the changes in monocytes, she has noted a rise in eosinophils, which has been almost a constant finding in our cases. I should like to know whether in the cases of Dr. Thomas in which there was apparent recovery the serum globulin has decreased. So far I have had opportunity to study only 1 such case and the globulin dropped with recovery. I have also found a rise in blood calcium, which cannot be explained by the height of the serum proteins. It does not occur only with changes in the bone; the word cyst is not accurate, since the cystlike area in the roentgenogram is a replacement of the marrow by the sarcoid lesion. It was interesting to note the widespread occurrence of amyloid in 1 of the cases

in which autopsy was performed. I had noted this in biopsy material but had been unable to stain amyloid in the microscopic preparations. In the only autopsy I have had an opportunity to study there were lesions in the liver and spleen of both sarcoid and typical caseous tuberculosis. I was able to recover tubercle bacilli by injection into animals of material from the caseous lesions but not from the other kinds. This would refute the idea that there is an unusual response on the part of the subject unless perhaps one happened to catch him in the state of change when the sarcoid lesions were beginning to disappear and the lesions due to tubercle bacilli were becoming more prominent.

DR. J. LAMAR CALLAWAY, Durham, N. C.: Recently my associate Dr. Paul G. Reque reviewed 20 cases of Boeck's sarcoid observed at Duke Hospital, in all of which the diagnosis was proved by biopsy. Four patients were white, 1 Indian and 15 Negro. In 19 cases roentgenograms of the chest showed enlargement of the hilar node, and in several there was evidence of extensive involvement of both lungs. Roentgenograms of the hands, feet and long bones were made in 18 cases, in 7 of which there were either definite areas of rarefaction or cystic formation; it is interesting that roentgenograms of the feet showed more cystic changes than those of the hands. In all 20 cases the globulin fraction was elevated and the albumin content either normal or decreased. There was a relative increase in monocytes in 5 out of 20 cases, the highest count being 16 per cent, but there was no correlation between the activity of the disease and the high monocyte count. Reactions to tuberculin tests were negative in 18 of the 20 cases; in 1 of the remaining cases there was a positive reaction to tuberculin in a dilution of 1:10,000 and in the other a 2 plus reaction to tuberculin in a 1:1,000 dilution. As in the cases reported by Dr. Thomas, almost every conceivable type of therapy, including fever therapy, was given without beneficial results. Three of the patients in this series showed a generalized grouped follicular eruption, widespread over the entire body, very similar to lichen scrofulosorum, and in all 3 the reactions to tuberculin tests were entirely negative. One of our patients showed sarcoid involvement of the eye which necessitated enucleation. In 1 patient the presenting symptoms and signs were referable to the central nervous system. This again emphasizes the systemic nature of Schaumann's disease.

DR. FRANCIS A. ELLIS, Baltimore: Jüngling adequately described osteitis tuberculosa multiplex cystica in 1919 (*Fortschr. a. d. Geb. d. Röntgenstrahlen* **27**:375, 1919), and in 1928 (*Beitr. z. klin. Chir.* **143**:401-475, 1928) he reported 9 cases and collected 46 from the literature. In the second report he stated that the lesions were not cystic and therefore substituted the term cystoides for cystica. Recently some American authors, principally orthopedists, have reported cases of so-called cystic tuberculosis as sarcoid of the bone, and they proved, at least in their cases, that the disease was due to the tuberculosis. They found the organism in the biopsy specimens and by culture, but of course the mistake was that they were describing cystic tuberculosis of the bone and not sarcoid. In 1940 I reviewed these cases (*Acta med. Scandinav.* **104**:221, 1940).

DR. PAUL E. BECHET, New York: I should like to ask Dr. Thomas what results she has achieved in the treatment of the Boeck type of sarcoid with gold and sodium thiosulfate. My results have been negative. I have observed a few instances in which the discoid type of lupus erythematosus and Boeck's sarcoid coexisted and in which aurotherapy resulted in a cure of the lupus erythematosus but had no therapeutic effect on the sarcoids. A year or so ago one of the patients to whom I had administered aurotherapy twelve years previously for an extensive

discoid lupus erythematosus of the face had also many typical lesions of Boeck's sarcoid on the arms, upper part of the chest and back. At that time the lupus erythematosus completely healed, but the gold and sodium thiosulfate had no effect whatsoever on the sarcoids. When she was seen twelve years later, her lupus erythematosus had remained well and had not recurred, but she had just as many sarcoids as before.

Dr. Fred D. Weidman, Philadelphia: One of the most recent additions to this subject appears in a communication by Schaumann and Hallberg entitled "Koch's Bacilli Manifested in the Tissue of Lymphogranulomatosis Benigna (Schaumann) by using Hallberg's Staining Method" (*Acta med. Scandinav.* **107:** 499, 1941). It is in English and carries colored illustrations of the tubercle bacilli in the tissue. Some of them were stained by acid-fast technic and some were not. The non-acid-fast ones were demonstrated by means of a new technic employing *Nachtblau,* by which method the micro-organisms stained blue. A feature in Dr. Thomas' presentation that struck me rather forcefully was the small proportion of white patients. Of course, in the European literature white patients predominate. In the United States it has been the experience of all, I am sure, that it is the Negro race that is predominately affected. I should like to ask Dr. Thomas whether she has broken down the data in her studies whereby there might appear certain differences, particularly in the matter of tuberculosis anergy, between the white and Negro subjects.

Dr. Walter C. Jones, Birmingham, Ala.: Has Dr. Thomas any evidence as to what part of the body is affected first? I ask this question because I have found out, by personal communication, that Dr. Longcope and his workers seem to think that this disease has its origin in the lungs.

Dr. Adolph Rostenberg Jr., Washington, D. C.: May I ask Dr. Thomas if she has ever used Nickerson's antigen? Those who were at the Atlantic Dermatologic Conference in Boston in 1941 will recall that there was some talk about the Nickerson intradermal test (Arch. Dermat. & Syph. **45:**412 [Feb.] 1942).

Dr. Carmen C. Thomas, Philadelphia: In answer to Dr. White I am glad to confirm his observations that various types of cutaneous lesions are often found in the same patient (for instance, lesions resembling lupus erythematosus on the scalp and erythema-induratum-like lesions on the leg), and they also seem to respond somewhat differently clinically (those on the scalp healing more rapidly perhaps than the others). In answer to Dr. Harrell regarding the question of eosinophilia, I have been unable to find significant changes in that direction. I observed 2 or 3 per cent eosinophils, I believe, in 3 patients but did not consider that particularly abnormal. Dr. Bechet mentioned the question of gold therapy. I tried that in about 3 cases with no effect whatever and therefore abandoned it in the other cases, perhaps too soon. I did not have time to bring out, as Dr. Weidman suggested, differences in the course of sarcoid in the white and the Negro race. I had the general impression that the disease in my 3 white patients was much more benign, in so far as it produced much less apparent widespread damage and less physical debility, but that is only an impression.

CONGENITAL EPIDERMAL CANALS OF THE PERINEAL RAPHE

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My attention was called to the possibility of congenital epidermal canals being responsible for chronic inflammation of the perineal raphe by the following case.

REPORT OF A CASE

An American of Bohemian ancestry, aged 23, was first seen on Feb. 7, 1939. He complained of several small but painful ulcers distributed along the under surface of the penis and the midline of the scrotum. He related that while working in the wheat harvest in the late summer of 1937 he noticed a small reddened lesion on the posterior aspect of the penis 2 or 3 inches (5 to 7.5 cm.) from the prepuce. He consulted a dermatologist, to whom the appearance suggested larva migrans and who prescribed calamine lotion for local application, but in a few months a new lesion appeared at the penoscrotal junction.

The patient consulted another physician, who made a diagnosis of local venereal infection (probably chancroid) and cauterized the affected areas with silver nitrate. Only temporary improvement was noted. In April 1938 the patient had a urethritis of the gonorrheal type, for which he consulted a third physician, who prescribed sulfanilamide by mouth and neo-silvol by injection. The discharge cleared promptly under this treatment, and by May of the same year the urethritis was pronounced cured.

The inflammatory condition along the ventral surface of the penis, however, showed no improvement; treatment consisted of freezing with solid carbon dioxide and applications of phenol. At this point the patient again consulted the dermatologist he had seen first, who now asserted that some venereal infection was complicating the clinical picture. He examined several smears, but no specific type of infection could be found. More abscesses continued to form along the midline of the scrotum, and the patient sought another dermatologist, who decided that the condition was a localized staphylococcic infection. The patient was given several roentgen ray treatments while in this physician's care, without apparent benefit; dressings consisting of various powders and gentian violet gave only temporary relief.

Examination revealed the patient to be well developed and normal physically except for a congenital dimpling of the chin. When the external genitals were inspected four draining fistulas were seen, two on the posterior raphe of the penis and two on the scrotal raphe. One fistula was located about 5 cm. from the meatus, and on pressure pus exuded from the opening. All of the tissues immediately about the lesion and along the perineal raphe proximally about 6 cm. to the perineoscrotal junction were reddened and indurated. There was a more extensive indurated area at the perineal line with a draining sinus slightly larger than the one below. A section for histologic study was removed from this region. The area of inflammation along the raphe was cordlike to the touch for a distance of 2 or 3 cm. in both directions. As the two scrotal lesions had been the last to

appear, they were much smaller than those on the penis, and there was little inflammatory reaction about them. An earlier lesion on the scrotum had been completely obliterated by previous electrodesiccation, the destruction being so deep that apparently it had destroyed a portion of the canal.

The diagnosis on first examination was chancroidal infection or lymphogranuloma venereum, but the reaction to a Frei test was negative and smears showed

Fig. 1.—Cordlike thickening of the perineal raphe produced by the chronic infection in the epidermal canal. One of the fistulous openings is noted in the center.

only pus cells and a few gram-positive cocci. Cultures in nutrient agar and Sabouraud's agar showed only Staphylococcus albus.

The first treatment consisted merely of bathing the lesions in a 1:8,000 solution of potassium permanganate and applying moist boric acid packs. Little change

was noted after two weeks of such treatment. The patient was then given azosulfamide (disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′, 6′-disulfonate), 30 grains (1.9 Gm.) daily for ten days, which produced temporary response by reduction of tenderness and a lessening of the exudate draining from the fistulas. Two of the abscesses were also treated by filtered roentgen rays in doses of 300 r each. Finally, with the area under local anesthesia, tissue was removed for histologic examination, and at the same time a small dull probe was inserted in the most distant of the penile lesions. It was discovered then that the probe could be passed as far as the fistulas at the penoscrotal junction. When the instrument was withdrawn and reinserted at the penoscrotal angle the canal proved to be patent all the way to the scrotum save in one area, where for 1 cm. the lumen had been destroyed by fulguration,

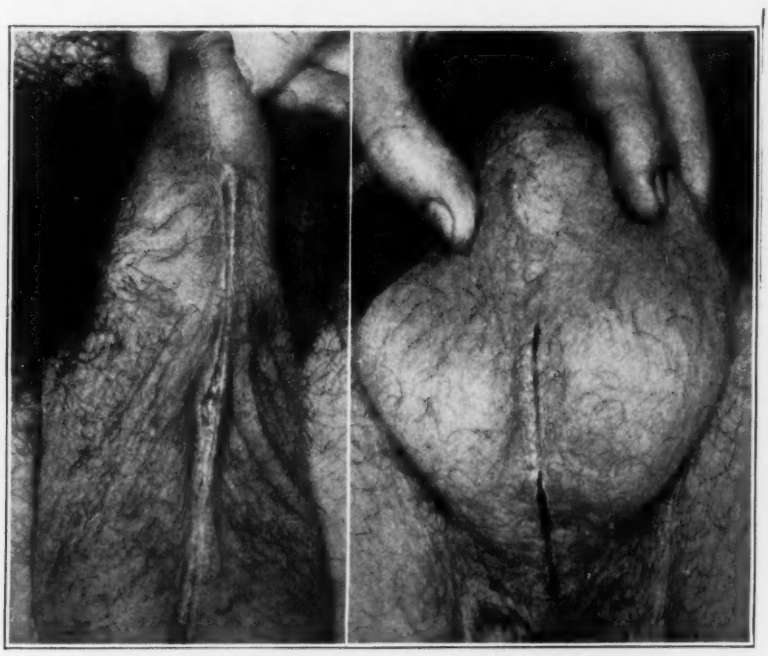

Fig. 2.—The entire embryonic tract has been incised by the cutting current and the epidermal canal destroyed by electrodesiccation.

as has already been noted. The diagnosis of congenital epidermal canal with secondary infection was thus made plain.

Treatment consisted of opening the canal throughout its entire length by electrodesiccation after anesthetization of the perineal raphe with procaine hydrochloride. The canal itself was destroyed together with the local abscesses. All of the wounds healed promptly, and recent examination showed nothing but a thin scar along the whole length of the perineal raphe.

A biopsy specimen from the larger sinus showed the surface epithelium to be acanthotic with enlargement of the papillary bodies. There was considerable acanthosis also at the edge of the fistulous openings where the rete was decidedly proliferated. Edema both within and without the cells, pyknosis of the nuclei, spongiosis and *altération cavitaire* were noted. Extravasation of blood was in

evidence at the edge of this sinus opening. The corium was filled throughout with a cellular infiltrate consisting of plasma cells and lymphocytes, with dilatation of the capillary spaces and a moderate degree of edema.

Deep in the corium (fig. 3) lay an epidermal canal formed of squamous cell epithelium of varying thickness which showed an inflammatory reaction similar to that already described, that is, spongiosis, edema and *altération cavitaire*. In

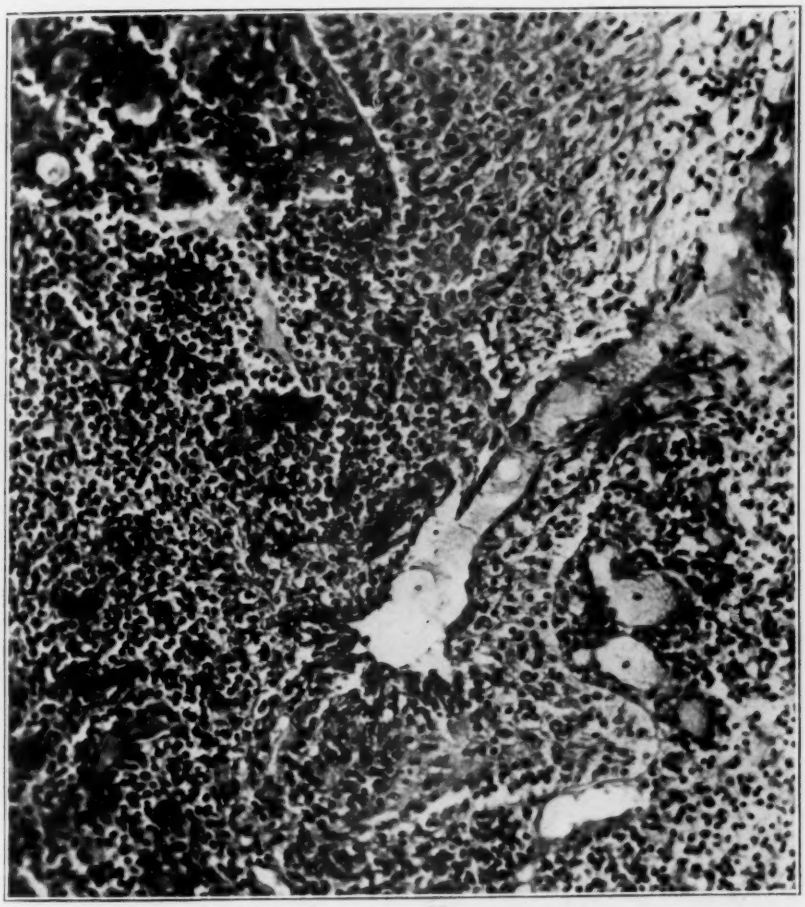

Fig. 3.—Inflammatory reaction in the congenital epidermal canal with edema and spongiosis. Also, note the lymphocytic and plasma cell infiltrate in the connective tissue surrounding the canal.

one place the basal cells were spindle shaped and elongated. The lumen of this canal was filled with a pink-staining reticular substance.

Another section removed from a noninfected area through which the probe had been passed showed a slight acanthosis and spongiosis of the surface epithelium. The connective tissue, however, was normal except that deep in the corium there was a continuation of the canal formed of stratified squamous epithelium. This epithelium (fig. 4) corresponded in structure to that of the epidermis. The prickle cell layer displayed intercellular edema, although the prickles were still in evidence.

This prickle cell layer blended with the squamous cell layer, where there was atypical keratinization with a moderate degree of parakeratosis.

EMBRYOLOGY

The genitoperineal raphe exists as a permanent surface marking indicating where the ventral or caudal midline fusion resulting in the

Fig. 4.—Epidermal canal removed from a noninflammatory portion of the median perineal raphe.

formation of the perineum, scrotum and urethra took place during embryonic development. Most students of embryology believe that the epithelium covering the under surface of the phallic projection deep in the urethral groove is merely an extension from that which lines the urogenital sinus. If this theory is correct the mucosa of the urethra is endodermal in origin except in its balanic portion. An epithelial plate which grows into the primitive glans as a solid column of cells, later

breaking down to form a groove, provides this balanic portion, which becomes one continuous canal with that formed earlier by fusion of the urethral folds. It is probable that with this process of fusion some epithelial cell aggregations might be enclosed in the plane of fusion, a process analogous to the origin of branchial cleft cysts. Such rests would later provide canals (or cysts if there was no opening on the cutaneous surface) lined with epithelium like that from which they originated. If the lining originated in the primitive urethra it would be endodermal or columnar; if from the level of the cutaneous surface or near it, ectodermal or squamous.

Another embryologic explanation has been offered by Johnson,[1] who showed that in an embryo 88 mm. long there were some cellular outgrowths from the penile urethra completely split off and some in the process of being divided from the main epithelium, both types being already canalized. Johnson considered this as factual evidence of the probable origin of periurethral ducts and cysts.

In the 11 cases studied by Gougerot, Burnier and Tissot [2] stratified epithelium was found in all but 2. Okawa [3] found this type of epithelium in 9 cases. This appears to be general, as it is mentioned in most of the articles concerning these anomalous formations which I have been able to review. The case reported here appears to be the thirty-fourth to be placed on record. In 1893 2 were reported by Balzer and Souplet,[4] while two years later Mermet [5] collected from the literature 23 cases of congenital cysts of the raphe. Rupel [6] reported 8 instances of epidermal canals in 1924 and Okawa 9 in 1929. Gougerot, Burnier and Tissot reviewed the whole subject in 1933 with consideration of 11 cases, while Neff [7] in 1936 brought the total number of cases of congenital cysts and canals of the perineal raphe up to 33.

DIAGNOSIS

As can be seen from the misadventures in my case, diagnosis is by no means easy. Chancroidal infections, multiple chancres of syphilis,

1. Johnson, F. P.: The Later Development of the Urethra in the Male, J. Urol. **4**:447, 1920; Diverticula and Cysts of the Urethra, ibid. **10**:295, 1923.

2. Gougerot, H.; Burnier, and Tissot: La blennorragie des canaux accessories sous-urétraux, Ann. d. mal. vén. **29**:641, 1933.

3. Okawa, S.: Ueber die chronisch gonorrhoeische Entzündung der Paraurethralgänge, Acta dermat. **14**:229, 1929.

4. Balzer, F., and Souplet: Deux observations de suppuration en trajet canaliculaire le long du raphé médian du pénis et du scrotum, Ann. de dermat. et syph. **4**:359, 1893.

5. Mermet, P.: Les kystes congénitaux du raphé génito-périnéal, Rev. de chirurg. **15**:382, 1895.

6. Rupel, E.: Epidermal Canals Infected with Gonococci, Surg., Gynec. & Obst. **39**:636 (Nov.) 1924.

7. Neff, J. H.: Congenital Canals and Cysts of the Genito-Perineal Raphé, Am. J. Surg. **31**:308 (Feb.) 1936.

lymphogranuloma venereum, lymphangitis, pyogenic abscesses and tuberculosis had to be considered and ruled out. A dark field examination was made in 1 of Neff's cases because what appeared to be the initial lesion made its appearance on the frenulum. Yet it would seem that confusion with syphilitic chancre in this case would be less likely, because the lesions were multiple, of long duration and apparently autoinoculable. In my case the edges of the small fistulous openings were ragged, not punched out and painful, whereas the initial chancre of syphilis gives no pain. Also, the dark field examination gave repeatedly negative results, and there was but trifling inguinal adenopathy. I considered chancroidal infection, but smears revealed only staphylococci. Two of the lesions, the one on the shaft of the penis and the one on the scrotum, were contiguous, which gave a suggestion of inoculation from one to another, but as the lesions followed along the median raphe this seemed peculiar.

The differential diagnosis from herpes progenitalis was easy, for this more often appears on the inner surface of the prepuce. Also, the duration of herpes is brief; there is little induration about the lesions, and multiple tiny vesicles closely grouped together will be observed in the early stages.

Lymphogranuloma venereum was suggested, but the lack of suppurative lymphadenopathy even when the infection had existed for many months and the negative reaction to the Frei test ruled this out.

Biopsy gave the supportive evidence of a congenital tract lined with squamous epithelium, but other clinical features provided important testimony, such as (1) the presence of induration and the cordlike appearance of the perineal raphe adjacent to the fistula; (2) the ability to pass the small probe down the canal between the fistulous openings, and (3) the history (in many cases besides my own) of gonorrhea. Although in my case, and in many others, the infection of the raphe preceded the gonorrheal attack and remained after the specific infection had been pronounced cured, cultures and smears in this case and in 1 of Neff's yielded Staph. albus.

COMMENT

An examination of dermatologic literature showed that scant attention has been given to congenital epidermal canals of the perineal raphe. Little more information was forthcoming from works on urology, but the condition is properly classed as an anomaly of the external male genitalia. For example, Lowsley and Kirwin [8] devoted only a brief paragraph to the subject, although most urologic anomalies are treated at considerable length. Its importance resides in the difficulties of diagnosis for derma-

8. Lowsley, O. S., and Kirwin, T. J.: Clinical Urology, Baltimore, Williams & Wilkins Company, 1940, vols. 1 and 2.

tologist and urologist alike in cases in which the congenital canals become infected with gonorrhea or nonspecific organisms gain entrance to them.

The only comprehensive review of recent years is the article by Neff,[7] to which brief reference was made by Sutton and Sutton.[9] According to Neff, congenital cysts and ducts along the perineal raphe have long been recognized as corresponding to defects in the embryologic development of the external genitalia, but two different explanations of their origin have generally been offered: (1) They arise from epithelial rests which result from incomplete closure of the urethral or genital folds, and (2) they develop from outgrowths of embryonic epithelium which split off after primary closure of the folds. As early as 1895 Mermet [5] reviewed 23 cases in which cysts and fistulas along the perineal raphe had become infected and thus called attention to their existence. This author laid special stress on the anomalous nature of the condition.

The following conditions may be grouped in one category: (1) dermoid cysts and epidermal canals of the perineal raphe; (2) accessory ducts of the penis and of the scrotum, and (3) ducts and cysts situated between the layers of the prepuce lined either with squamous or cylindric epithelium or occasionally with cell structure of both kinds. Schoenhof [10] cited a case, also cited by Jadassohn, in which there was a congenital duct of the prepuce showing squamous epithelium at its beginning and farther down in the duct a cylindric cell structure.

TREATMENT

The simplest and surest treatment of congenital canals of the perineal raphe is excision or, better still, incision with the electric cutting current along the course of the canal, in the lumen of which a probe has been inserted. The canal itself should be destroyed by electrodesiccation, or if it lies deep excision of the entire tract would be more satisfactory.

SUMMARY

1. Persistent fistulas of the perineal raphe are reported in a case of congenital epidermoid canal of the perineal raphe.

2. Thirty-three cases previously reported in the literature were reviewed.

3. Treatment is either by excision or incision and destruction of the epidermal canal.

Medical Arts Building.

9. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939.

10. Schoenhof, S.: Gonorrhoische Infektion akzessorischer Gänge des Penis und Scrotum, Arch. f. Dermat. u. Syph. **155**:132, 1927.

NODULAR NONSUPPURATIVE PANNICULITIS

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AND
ROBERT A. KRITZLER, M.D.
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The purpose of this paper is to report the results of the first autopsy of a patient who died with acute lesions of relapsing febrile nodular nonsuppurative panniculitis. This disease is characterized by recurring attacks of fever, accompanied by the development of nodular nonsuppurative lesions of the panniculus adiposus, and healing by fibrosis leaving visible depressions in the surface of the skin if the lesions were of sufficient size. Histologic study shows necrosis of the fat cells, an interstitial exudate predominantly of lymphocytes and phagocytosis of fat both within and between the fat cells. The destroyed fat may be replaced by fibrous tissue.

The autopsy observations to be reported may or may not be a part of the syndrome but will serve as a guide for future observations of patients with this as yet unusual and obscure disease.

To date reports of 26 more or less typical cases of this disease have been published. Twenty-one of the patients were women, and 5 were men. Pfeifer [1] in 1892 reported the first case, pointing out that similar changes of the adipose tissue could be induced artificially. In 1916 Gilchrist and Ketron [2] reported the second case, that of an 8 year old girl, emphasizing the role of the macrophage in the lesion. Weber,[3] in reporting the third case in 1925, supplied the name which, with the addition of "febrile" by Christian [4] in the fourth case in 1928, is still

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Read before the Section on Dermatology and Syphilology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

1. Pfeifer, V.: Ueber ein Fall von herdweiser Atrophie des subcutanin Fettgewebes, Deutsches Arch. f. klin. Med. **50**:438-449, 1892.

2. Gilchrist, T. C., and Ketron, L. W.: A Unique Case of Atrophy of the Fatty Layer of the Skin, Preceded by the Ingestion of the Fat by Large Phagocytic Cells—Macrophages, Bull. Johns Hopkins Hosp. **27**:291-294 (Oct.) 1916.

3. Weber, F. P.: A Case of Relapsing, Nonsuppurative Nodular Panniculitis, Showing Phagocytosis of Subcutaneous Fat Cells by Macrophages, Brit. J. Dermat. **37**:301-311 (July) 1925.

4. Christian, H. A.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, Arch. Int. Med. **42**:338-351 (Sept.) 1928.

used. Alderson and Way [5] reported the fifth and Netherton [6] the sixth case. Weber,[7] in reporting the seventh case, suggested iodides as the probable cause in this case, as the onset followed ingestion of iodides and a recurrence coincided with a second administration of them.

In April 1940 Tilden, Gotshalk and Avakian [8] summarized additional cases by Brill,[9] Bailey,[10] Reed and Anderson,[11] Cummins and Lever,[12] Shaffer [13] and Binkley.[14] They added 2 cases of their own, bringing the total to 20.

Since then 6 additional reports have appeared. Hazel and Lamb [15] in January 1940 reported the case of an 11 year old girl with lesions on the abdomen and legs. One of the lesions clinically resembled morphea. The patient was afebrile while observed, but otherwise the findings were typical of this disease. Ziegert [16] in September 1940 reported the case of a 34 year old woman with two palm-sized lesions on the chest and abdomen and smaller lesions in the left axilla and on the arms. Fever and leukopenia were present. The histologic observations reported conform with those made in other cases of this disease.

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5. Alderson, H. E., and Way, S. C.: Relapsing Febrile Nonsuppurative Panniculitis (Weber), Arch. Dermat. & Syph. **27**:440-449 (March) 1933.

6. Netherton, E. W.: Relapsing Nodular Nonsuppurative Panniculitis, Arch. Dermat. & Syph. **28**:258-259 (Aug.) 1933.

7. Weber, F. P.: A Further Note on Relapsing Febrile Nodular Nonsuppurative Panniculitis, Brit. J. Dermat. **47**:230-233 (June) 1935.

8. Tilden, I. L.; Gotshalk, H. C., and Avakian, E. V.: Relapsing Febrile Nonsuppurative Panniculitis, Arch. Dermat. & Syph. **41**:681-689 (April) 1940.

9. Brill, I. C.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), in Medical Papers Dedicated to Henry Asbury Christion in Honor of His Sixtieth Birthday, Baltimore, Waverly Press, Inc., 1936, pp. 694-704.

10. Bailey, R. J.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), J. A. M. A. **109**:1419-1424 (Oct. 30) 1937.

11. Reed, A. C., and Anderson, H. H.: Relapsing Nonsuppurative Panniculitis, California & West. Med. **47**:325 (Nov.) 1937.

12. Cummins, L. J., and Lever, W. F.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), Arch. Dermat. & Syph. **38**: 415-426 (Sept.) 1938.

13. Shaffer, B.: Liquefying Nodular Panniculitis, Arch. Dermat. & Syph. **38**:535-544 (Oct.) 1938.

14. Binkley, J. S.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, J. A. M. A. **113**:113-116 (July 8) 1939.

15. Hazel, O. G., and Lamb, J.: Primary Panniculitis Afebrile in Type and Associated with Sclerodermatosis-Like Changes, J. Oklahoma M. A. **33**:1-5 (Jan.) 1940.

16. Ziegert, H. J.: Ein Fall von fieberhafter Wucheratrophie des Fettgewebes (Weber-Christian'sche Krankheit), Zentralbl. f. inn. Med. **61**:610-612 (Sept.) 1940.

Skiöld [17] in 1940 described a clinically typical case. The patient was a 51 year old woman with lesions beginning on the lower extremities and fever, her temperature reaching 40 C. (104 F.). During the course of a year some lesions healed with depression of the cutaneous surface, but new lesions continued to form. A purulent infection of the teeth, necessitating the extraction of fourteen teeth, was accompanied by a distinct increase in the number of new lesions and a temperature of 37.7 C. (99.9 F.).

Hartwell and Thannhauser [18] reported the case of a 32 year old white woman whose lesions began on the shins and soon spread over the back, abdomen, breasts and neck. When first observed she had, in addition to the nodules, acute pericarditis and pleural effusion. She had a temperature as high as 103 F. Laboratory studies showed lowered serum protein, serum albumin and serum cholesterol. Crusting was present over two of the nodules. There was gradual improvement, and after six admissions to the hospital she had gained 43 pounds (19.5 Kg.) in weight. No evidence of cardiac changes were present, and the nodules had healed, leaving depressed areas.

The case of a 28 year old white man with recurring lesions on the right leg was reported by Hanson and Fowler.[19] Their patient showed slow healing of the wound made for removal of a biopsy specimen and the unusual feature of spontaneous rupture of a lesion on the calf.

Larson and Ootkin [20] reported the case of a 58 year old man who was observed with a number of painful nodules on the chest, back, thighs and arms. The histologic picture was typical. He was observed for eight months without recurrence.

The outcome in these 26 reported cases was as follows: One died apparently from the disease. Another, six months after observation for panniculitis, died of acute tuberculosis with no autopsy evidence of active lesions of panniculitis. Four patients were observed ten to fourteen years, during which time a number of relapses occurred, and only 1 had been free of lesions for a reasonable time at the last report. The remainder of the patients either had active lesions when last reported on or had not been followed long enough to rule out subsequent relapses.

17. Skiöld, N.: Relapsing Febrile Nonsuppurative Panniculitis, Acta med. Scandinav. **105**:43-47, 1940.

18. Hartwell, A. S., and Thannhauser, S. J.: Case Presentation and Discussion of Relapsing Febrile Nodular Nonsuppurative Panniculitis, Bull. New England M. Center **2**:362-368 (Dec.) 1940.

19. Hanson, W. A., and Fowler, L. H.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, Minnesota Med. **24**:779-782 (Sept.) 1941.

20. Larson, C. P., and Ootkin, B. N.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian's Disease), Am. J. Clin. Path. **11**:781-787 (Oct.) 1941.

The following case is the twenty-seventh to be reported, and because of the unusual severity and fatal outcome the report is given in detail.

REPORT OF A CASE

History and Course.—A Jewish housewife aged 34 was admitted to the clinic on Aug. 26, 1940, complaining of fever, malaise and a tender depressed area on the right thigh of seventeen months' duration. There was no history of tuberculosis, syphilis or chronic illness in the family. She was the mother of two children living and well. The past history was significant in that she had dieted for five years to prevent gain in weight. She had also taken "jad salts," "kreuschen salts" and "espotabs." The patient had enjoyed excellent health until January 1939, when an infected tooth was extracted. Extraction was particularly difficult, and a month was required for healing, during which time blood and pus issued from the socket several times. Two months later (March) she had a fever, with a temperature up to 102 F., lasting for five days and five or six pea-sized, nontender nodules appeared on the lateral aspect of the right thigh. No further notice was taken of these lesions until November, at which time the early nodules had become confluent and now presented the picture of a red, slightly tender, raised area 4 inches (10 cm.) in diameter. She received various local treatments for "varicose veins" from December to July 1940, at which time a daily temperature of 101 F. was noted, although she remained in bed for five weeks.

On admission to the clinic in August 1940 she showed a red, mildly tender area of induration 10 cm. in diameter on the lateral aspect of the right thigh. The center of this lesion was strikingly depressed, and the edges were slightly elevated. Several smaller nodular lesions, 1 to 2 cm. in diameter, were scattered about the main lesion. Also extending out from the main lesion were several indurated cords. Aside from the nodular lesions on the thigh and a temperature of 101 F., physical examination revealed nothing striking. An examination in the endocrine clinic showed no evidence of endocrine dysfunction.

The basal metabolic rate was —5 per cent. The total cholesterol and its partition, the iodide content of the blood and the urine were normal. No bromides were found in the blood, and the cell count was normal. Roentgenograms of the sinuses and the right thigh showed no abnormality. A blood culture showed no growth. The Wassermann reaction of the blood was negative.

A section of tissue from the edge of the lesion on the right thigh was removed. Direct smear and cultures gave negative results. Histologic examination by Dr. Gerald F. Machacek revealed a slight hyperkeratosis of the epidermis with vesicular cells. The nuclei were surrounded by a clear space. The papillary and upper reticular parts of the cutis were the sites of increased cellularity and edema. The manifestations increased in intensity with the depth of the specimen. In the deep part of the cutis and subcutaneous fat there was an infiltration of round mononuclear cells. Areas of fibrous tissue proliferation were noted. The adipose tissue had undergone necrosis. Lipophages were present. There was a thickening of the vessel walls but no recognizable obliteration of the lumens of the large vessels. The changes were maximal in the fat tissues. Evidently the lesion was a panniculitis.

The extraction of an impacted tooth on Nov. 9, 1940 was followed by fever, with a temperature of 103 F., and chills. One week later new lesions appeared on the right thigh and for the first time lesions began on the left thigh. Six weeks was required for healing of the gum.

By Jan. 8, 1941 the patient had a daily temperature of 104 F. and new lesions were present on the legs and over the sacrum. She was complaining of pains in shoulders and legs and general weakness. At this time the administration of sulfanilamide was started by mouth. Sixty grains (4 Gm.) was given for three days, 40 grains (2.6 Gm.) for two days and 10 grains (0.65 Gm.) for two days. The temperature fell from 104 to 101 F. by the sixth day, the lesions appeared less red and the patient's general condition improved. Administration of the drug was stopped for two days. When it was given again fever (temperature of 105 F.) appeared and the patient was admitted to the hospital on January 19.

Physical examination revealed no abnormalities except the nodular lesions described in the subcutaneous tissue, enlarged tonsils and a discharge from the unhealed wound made for removal of a specimen for biopsy. The liver and spleen were not palpable. A roentgenogram of the chest was normal. Agglutination for hemolytic streptococci group A, Brucella abortus and Brucella melitensis

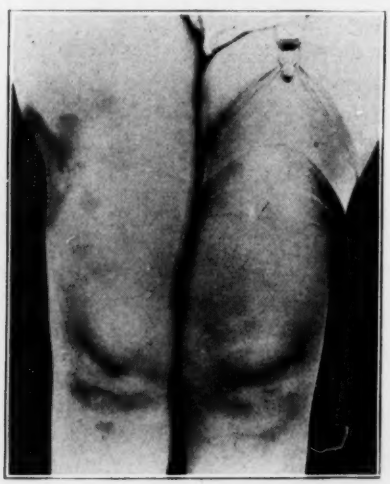

Fig. 1.—Distinctly depressed area on the right thigh at the site of a lesion undergoing involution and several satellite subcutaneous nodules.

showed no agglutination. Numerous blood cultures showed no growth except for occasional obvious contaminants. The total protein content of the serum and its partition and the nonprotein nitrogen content of the serum were normal. Various studies of the teeth showed no foci of infection.

The patient was given 3.6 Gm. of sulfanilamide daily for seventeen days with maintenance of a daily level of 4 to 6 mg. of free sulfanilamide per hundred cubic centimeters of blood.

No new lesions developed while the patient was in the hospital. She was discharged on February 13 but was readmitted on February 19 because new lesions appeared on the buttocks. During the first nine days of her second admission the patient was given 6 Gm. of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) daily, with maintenance of daily levels of 4.0 mg. free and 6.0 mg. total per hundred cubic centimeters of blood. The administration of sulfathiazole was discontinued because of the possibility that the fever might have been caused by the drug. However, the fever continued after use of the drug was stopped and new lesions appeared.

Two and four-tenths grams of sulfanilamide was again given daily for two weeks beginning March 9. A cephalin flocculation test showed a 1 plus reaction. Sedimentation rates were normal. Cultures of material from the wound made for removal of a specimen for biopsy showed Streptococcus viridans.

The patient was discharged on March 25 and remained at home until May 12, when she was admitted to the hospital for the third time. During her stay at home new lesions appeared, and for the first time superficial ulceration appeared in a number of lesions on the back and legs. Night sweats began, and a tem-

Fig. 2.—Multiple subcutaneous nodules on the lower part of the back, buttocks and thigh, showing erythema and beginning crusting of several lesions.

perature up to 104 F. continued. Intracutaneous tests with old tuberculin 1 : 10,000 and with staphylococcus and streptococcus toxins gave negative results.

On the patient's third admission to the hospital physical examination showed a thin, high-colored, flushed, perspiring woman who seemed acutely ill. Many nodular lesions of varying sizes were present on the back, buttocks and legs. Some were small areas covered with reddened skin; others were denuded of epidermis. The liver and spleen were not palpable. The pulse rate was 175 to 190. Serum inorganic phosphorus and nonprotein nitrogen were normal. A bromsulphalein test showed retention at thirty minutes of 60 per cent of the dye. Serum phosphatase was 6.6 Bodansky units. The cholesterol content was 168 mg. per

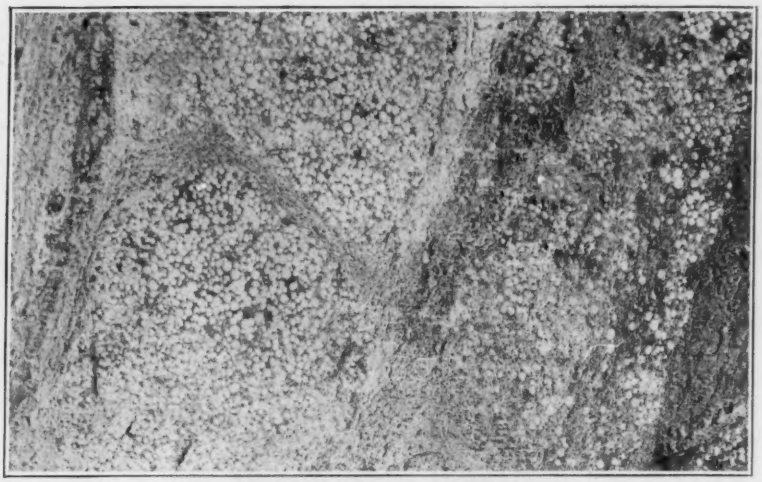

Fig. 3.—Section of the panniculus adiposus of the right thigh taken at autopsy showing necrosis of the fat and a widespread inflammatory exudate (× 60).

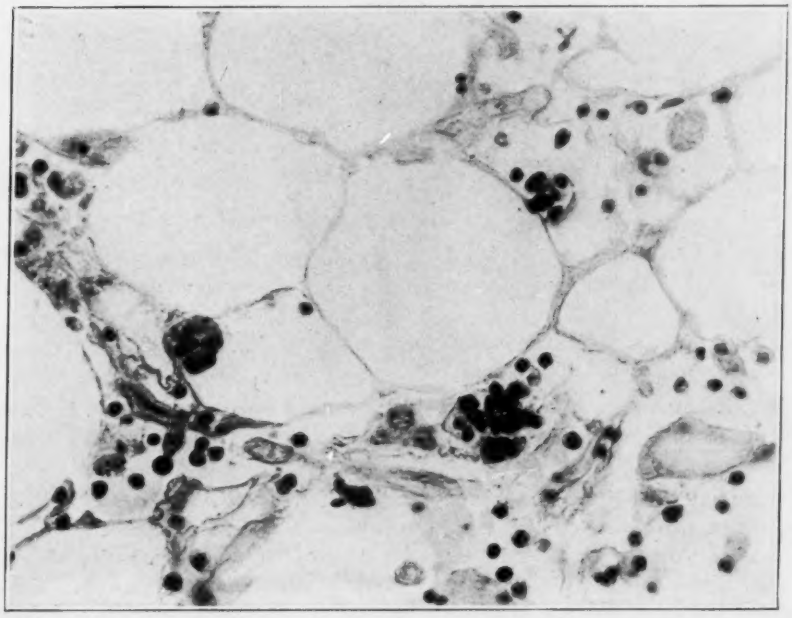

Fig. 4.—Section showing the lymphoid character of the exudate and the invasion of the fat cells by both phagocytes and lymphocytes. The cell membranes of some of the fat cells are partially collapsed inward. Lymphocytes are being phagocytosed within the fat cells (× 460).

hundred cubic centimeters; the proteins amounted to 6.2 per cent, with albumin 3.5 per cent and globulin 2.7 per cent. The reaction to a cephalin flocculation test was 3 plus.

Five blood transfusions were given from May 14 to May 29. A total of 24 Gm. of sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) was given from May 19 to 28, with no effect. The serum albumin content continued to fall, to 2.4 per cent. The serum cholesterol esters also continued to fall, finally reaching 10 per cent. Electrocardiographic studies showed a sinus tachycardia. The menses were absent for two months. New typical lesions developed on the arms during

Fig. 5.—Section showing ulceration of epidermis and nonsuppurative inflammation and necrosis around the sweat glands (× 90).

the week preceding death, but the skin over the majority of the old lesions was superficially ulcerated. No jaundice was ever present. The patient continued to have a fever, with a temperature up to 105 F., and a pulse rate of 150 or above. She retained consciousness until just before death. She died, apparently from general exhaustion and hepatic failure, on June 5.

Report of Autopsy.—Gross Observations: The autopsy was performed one and one-half hours after death. The body was moderately well nourished. Cutaneous lesions were mainly on the arms, thighs, buttocks and back. There were discrete

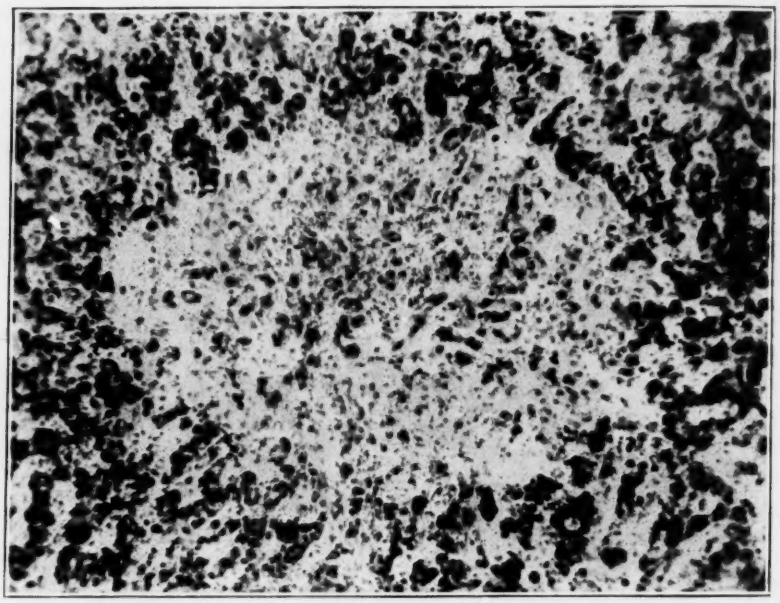

Fig. 6.—Fat stain of a section from the liver showing necrosis in the central zone and the accumulation of a moderate amount of fat in the liver cells of the peripheral portion of the lobule (× 110).

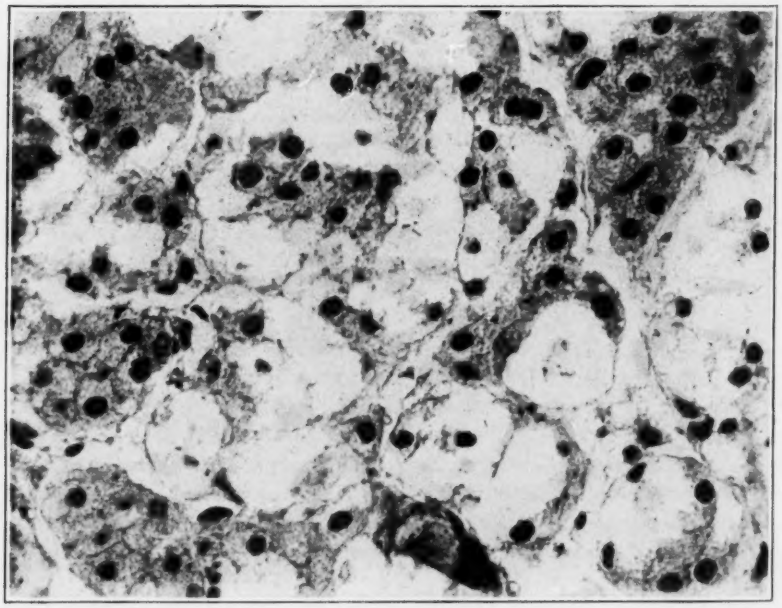

Fig. 7.—Section of the adrenal cortex showing hydropic degeneration of cells of the fascicular zone. These greatly distended cells have water clear cytoplasm and compress the sinusoids (× 460).

or confluent pinhead-sized blue areas varying from 1 to 5 cm. The underlying panniculus was of normal thickness and consistency. On the right thigh laterally there was an irregular area measuring 15 cm. where the panniculus was atrophied and firm. The overlying skin was sunken and bluish violet. The edges were slightly raised, nodular and red. On both thighs and arms there were several smaller, ill defined, slightly firm areas of panniculus over which there was reddish brown crusting. One of these on the right thigh was ulcerated. Here the dermis was exposed. The underlying panniculus was gray, thin and softer than normal. The edges of the unhealed wound made for the removal of a specimen for biopsy on the right thigh sagged into a soft, yellowish gray panniculus. In areas varying from 2 to 15 cm. in diameter on the back, buttocks and thighs, superficial layers of the epidermis were denuded, leaving gray, moist surfaces. Shallow decubitus ulcers were found in areas of pressure on the back. The liver was palpable 2 cm. below the costal margin. Adjacent to the rectum there was an abscess cavity measuring 1 by 1.5 cm. which communicated with the skin near the anus.

Examination was limited to the study of one cutaneous lesion and the organs of the abdomen and chest. The abdominal panniculus was yellow and of normal thickness. The perirenal, mesenteric and pericardial fat was abundant and normal grossly. The heart and aorta revealed no changes. There was a slight patchy atelectasis of the left lung but no areas of consolidation. The spleen weighed 360 Gm. Except for the enlargement it was normal grossly. The liver also was enlarged moderately, weighing 2,440 Gm. The cortical lipid of the adrenals was reduced moderately. The kidneys, pelvic organs, esophagus and stomach were normal. There was a small reddish superficial ulceration of the mucosa of the first part of the duodenum. Several calcified mesenteric lymph nodes were noted.

Microscopic Observations: Histologic examination of tissue from the right thigh showed that the panniculus adiposus was infiltrated widely by lymphocytes and small phagocytes containing fat vacuoles. The latter rarely assumed the appearance of foam cells. Some of the fat cells were well preserved, but large numbers were undergoing necrosis. As the cell membranes ruptured and collapsed inward, the fat cells became irregularly shaped and often reduced to flat spaces. Lymphocytes and phagocytes commonly invaded the fat cells, where they oriented themselves along the inner surface of the cell wall and underwent necrosis. Both within the fat cells and in the interstitium many of the phagocytes had distended themselves with lymphocytes and occasional red cells. Polymorphonuclear leukocytes were rare; there were no epithelial or giant cells. Lymphocytes and occasional wandering cells surrounded and invaded the walls of small vessels. These vessels also showed endothelial hyperplasia, edema of the walls and slight swelling of the elastic fibers.

The collagen of the dermis was dense but not swollen. The fat around the sweat glands showed the changes taking place in the panniculus. The vessels and hair follicles in the dermis were also surrounded by exudate. The epidermis was ulcerated.

Gram, Levaditi and Giemsa stains revealed cocci and bacilli in the necrotic debris of the ulcer. No organisms or fibrin deposits were seen in the panniculus. Scarlet red and osmic acid stains for fat showed that many of the fat cells contained only small amounts of fat taking the dye. Vacuoles in some phagocytes did not retain the fat dye. Fat taking the stain was commonly found in the tissue spaces. The skeletal muscle beneath the lesion on the thigh showed only moderate edema. The skin and the panniculus of the abdomen showed only rare phagocytes containing lymphocytes and also occasional collapsed fat cells in which there were phagocytes. The heart was normal except for occasional lymphocytes and phago-

cytes in the epicardial fat. A lymphocyte-laden phagocyte was noted in the adventitia of the aorta. Staining of the lung for fat revealed several fat emboli impacted in the pulmonary capillaries. The spleen contained acute, early focal necrosis. The reticuloendothelial cells were tremendously enlarged owing to ingestion of red cells. The sinusoids were congested, the malpighian bodies edematous and the pulp hemorrhagic. There were also areas of acute focal necrosis in the liver; these were mainly central. The sinusoids were frequently partially blocked by greatly enlarged Kupffer cells which had engorged themselves with red cells. Stains for fat showed the accumulation of a moderate amount of fat in the periportal zones. In the adrenal cortex cells of the fascicular and reticular layer had undergone hydropic degeneration. They were greatly swollen and were packed together tightly. The cytoplasm was water clear. Stains for fat showed that these cells contained no fat. The cortical lipid was reduced. Except for containing a few hemoglobin casts, sections from the kidneys were normal. Sections of peripancreatic, perirenal and mesenteric fat showed no necrosis or exudate. The pancreas, bladder, ovaries, small intestine, colon and diaphragmatic and psoas muscles were normal. A smear of material from a small perirectal abscess showed the flora of the lower bowel. Culture of material from the ulcer on the thigh showed Bacillus aerogenes and hemolytic Staphylococcus aureus. No anaerobic fungi were cultured.

COMMENT

The case herein described, we believe, agrees in essential clinical and histologic characteristics with the cases reported in the literature. When first observed the resemblance of this disease to morphea was striking. This resemblance was noted by Gilchrist and Ketron in the second reported case and again by Hazel and Lamb. The differential diagnosis from other cutaneous lesions has been adequately discussed by other writers.

In the subsequent course this case resembles those of Christian, Hartwell and Thannhauser, and Bailey's first case, in which high fever and severe constitutional symptoms were present. Bailey's patient died after one year's observation, but permission for autopsy could not be obtained.

The cause of this disease is still obscure. Three factors have been suggested by others as being of possible etiologic significance: 1. Iodides and bromides. In this case there was no history of ingestion of either, and examination of the blood for bromides was negative and for iodides within normal limits. 2. Foci of infection. Infected teeth have been present in over half the cases. Cummins and Lever stated that they considered this focus of no significance. Skiöld reported a distinct exacerbation in his case following fourteen extractions. In our case, the onset of the nodular lesions followed in two months the extraction of an infected tooth, and a severe relapse with fever and many new lesions followed a week after the extraction of another tooth. 3. Avitaminosis. Evidence of this has been an inconsistent finding in the

reported cases. Except for a history of dieting for five years without any gross evidence of malnutrition or vitamin deficiency this factor was not present in this case.

The failure of sulfonamide compounds in this case adds another point against the disease's being of infectious origin.

No successful treatment of this disease has so far been found. In our case the sulfonamide compounds were given a thorough trial. This therapy was not started until after several months of observation, at which time it was evident that we were dealing with a severe form of this condition with fever (temperature of 104 F.), general weakness and rapid development of new lesions. Sulfanilamide, sulfathiazole and sulfadiazine were all used at different times. They were given under the close supervision of Dr. Kneeland, of the department of medicine. Careful clinical observation for any possible sign of drug reaction was checked by daily blood counts and determinations of levels of the drug in the blood. In retrospect we think it may be stated definitely that the sulfonamide compounds were of no value in this case. An early apparent clinical improvement from sulfanilamide was not confirmed by subsequent use of this or related drugs. The question of whether these drugs were harmful to the patient must be weighed. In fairness, it must be emphasized again that the severe form of this disease was present before administration of the drugs was started. On the other hand, there is evidence that certain of the milder forms of this disease even with fever may have been caused by ingestion of iodides. Perhaps, then, any drug, including the sulfonamide compounds, might have had a harmful effect. In Bailey's fatal case the patient received neoarsphenamine, gold sodium thiosulfate and gentian violet intravenously. Christian did not report the therapy used.

Leukopenia, found in this case, was present in 5 others, but leukocytosis was reported in an equal number of cases.

In respect to the principal histologic features, namely, a nonsuppurative inflammation, necrosis of fat of the panniculus and the replacement in some advanced lesions of the fat by fibrous tissue, the lesions of this case are similar to those described. Ulceration of the epidermis, not previously described, did not occur until two months before the patient's death. At this time superficial ulceration of the skin began to appear in the more active lesions on the lower extremities and back. Subsequently most of the lesions over the entire body showed this change, but even terminally there were small new nodules present without ulceration. We interpret the ulceration as due largely to the pressure of the local subcutaneous lesion and to the general debility of the patient. Pfeiffer and Brill observed lymphocytes within the fat cells, as was found in this case, but in none of the cases so far reported

has the striking phagocytosis of lymphocytes both within and between the fat cells been recorded. A few or large numbers of giant cells have been described in the lesions of 9 patients, but they were not present in this case.

The autopsy failed to disclose any significant lesions of the fat in grossly uninvolved areas of the panniculus and in the inner depots. The fat emboli in the lungs are interpreted as due to entry into the blood stream of fat from the areas of lipolysis in the panniculus. Accumulation of fat and necrosis of the liver were of particular interest because of the laboratory evidence of rapidly increasing hepatic damage during the three weeks before her death. It is possible only to speculate as to any association of these changes with the lesions in the panniculus. Hepatic function tests in the other fatal case were reported by Bailey as giving normal results. In Christian's case there was one attack of unexplained jaundice. Both of these nonspecific changes in the liver could be due to other causes. A moderate fatty liver is not uncommon in persons who have had a poor food intake and high fever. The sulfonamide compounds must be considered as a cause for the hepatic damage. Garvin,[21] Russell [22] and Spring and Bernstein [23] have reported necrosis of the liver or hepatitis due apparently to sulfonamide drugs. In all of these cases there was jaundice, which was conspicuously absent in our case in the face of extreme damage of the liver cells. There are no reports of splenic necrosis due to the drugs, which was found in our case. Splenomegaly, present in this case, was also reported by Brill. The hydropic degeneration of the adrenal cortex cells is an uncommon lesion and should be looked for in future studies.

Fixed members of the reticuloendothelial system in the liver, spleen and bone marrow were filled with large numbers of red cells. Whether the phagocytosis of the red cells represented some abnormality of the reticuloendothelial cells in the liver, spleen or bone marrow in their normal response to altered red cells cannot be determined. Clinical and anatomic evidence for a transfusion reaction, a possible basis for increased destruction of red cells, is lacking.

The internal lesions found in this first autopsy were nonspecific, and only future postmortem studies of patients with this disease will determine their significance.

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21. Garvin, C. F.: Toxic Hepatitis Due to Sulfanilamide, J. A. M. A. **111**: 2283-2285 (Dec. 17) 1938.

22. Russell, H. K.: Acute Toxic Necrosis of the Liver Following the Use of Sulfanilamide, Ann. Int. Med. **14**:168-170 (July) 1940.

23. Spring, M., and Bernstein, I.: The Coexistence of Toxic Hepatitis, Acute Hemolytic Anemia, and Renal Damage Following Sulfanilamide Therapy, Ann. Int. Med. **14**:153-164 (July) 1940.

SUMMARY

The observations of the first autopsy to be performed on a patient who died with active lesions of relapsing febrile nodular nonsuppurative panniculitis are recorded. They include accumulation of fat and focal necrosis of the liver, hydropic degeneration of the adrenal cortex cells and the presence of large numbers of red cells in the fixed members of the reticuloendothelial system. The failure of the sulfonamide compounds to have a favorable influence on the course of the illness is emphasized. Ulceration of the skin over the subcutaneous lesions and phagocytosis of lymphocytes in the lesions in the panniculus adiposus are recorded for the first time. The cause of the disease remains obscure.

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ABSTRACT OF DISCUSSION

DR. LORETTA JOY CUMMINS, Boston: Drs. Miller and Kritzler have made an interesting contribution to the study of this puzzling syndrome. This disease cannot be considered lightly, as there are now records of 2 of the 26 reported cases terminating in death. Sulfonamide drugs were given a thorough test in this case, but since the results of blood cultures and practically all of the laboratory studies were negative, it is not surprising that there was no response to the use of these drugs. The authors state that Drs. Cummins and Lever do not feel that focal infection is of significance in this condition. That opinion was based on the study of 2 cases, both patients being girls 10 years old. There was some dental caries but no deep infection, apical abscesses or other foci of infection that could be found. Focal infection, named a factor in more than 50 per cent of the reported cases, must be given serious consideration. In the authors' case the disease definitely started after the extraction of an abscessed tooth, and there was a recurrence after an impacted tooth was removed. I do not feel that focal infection or ingestion of drugs, particularly bromides and iodides, which have been reported in several cases, is the causative factor, but I believe that one of these may be the exciting or precipitating factor and must be given consideration in the study of all future cases. I checked on the 2 cases which I reported, and there has been no recurrence of the condition in four years and the larger depressions remain the same as they were.

DR. WILLIAM A. ROSENBERG, Chicago: I had the opportunity to study 2 cases of panniculitis limited to the lower extremities. These cases were reported in the *Illinois State Medical Journal*. One of these was the case of a young woman who complained of a disturbance of the gallbladder, and because she was rather nervous she was given sodium bromide, 15 grains (1 Gm.) three times a day. She was watched for about three months, and no cutaneous lesions developed. She was then given a reducing diet, and in about three months she lost 30 pounds (13.6 Kg.). While on the reducing diet she did not receive any medication, but when the nodules developed on the lower extremities she was transferred to the dermatologic department. A clinical diagnosis could not be made. However, histologically the nodules proved to be lesions of the Christian-Weber syndrome. The interesting feature was that the lesions did not develop while she was taking bromides; in fact, they developed while she was not taking any drugs, and after that they could be precipitated whenever she was given 15 grains of sodium bromide.

I wonder whether being on a strict diet and making a rapid reduction in weight may not disturb the local fat metabolism and thereby precipitate this particular syndrome when a drug is administered.

Dr. Fred D. Weidman, Philadelphia: Dr. Miller sent me sections from both the internal organs and the skin. I found the picture of a panniculitis, and a feature of it that struck me forcibly was the extreme necrosis of the tissue, that is, as if there were some powerfully acting toxic factor in the case, such as is produced by bacteria rather than the kind which is commonly produced by drugs. I was also able to find two very small granulomas, and this finding made me think of the possibility of erythema nodosum or, if not that, the order of reaction that is seen in erythema nodosum. It is true that there is not much of a spread between the type of reaction of panniculitis and erythema nodosum, but the closer one studies erythema nodosum, the more one realizes that it is an acute inflammatory reaction. That is borne out by the clinical and other data in this case; there was high temperature. There was the extraction of a tooth and there was a septic focus; so perhaps this condition is rather intermediary between a process of the order of erythema nodosum and one of the order of a panniculitis. Perhaps that is the explanation in this case for the unusual circumstance, that is, the fact that there was a preceding acute inflammatory condition.

Dr. J. Lowry Miller, New York: Dr. Cummins aptly explained the use of sulfonamide drugs in this particular case. Drastic treatment was necessary, as the patient was extremely ill. The sulfonamide compounds had never been tried, and there is considerable evidence that perhaps panniculitis is of infectious origin. The drugs produced absolutely no beneficial results in this case. As regards the histology, I regret that Dr. Kritzler is prevented by military duty from being present to discuss this with Dr. Weidman. Clinically there was no relationship with the usually accepted type of erythema nodosum and the picture was typical of panniculitis. Dr. Rosenberg's remarks concerning the possible significance of the stringent reducing diets his patients had been on are of interest. Our patient had been on that type of diet for five years. Dr. Ketron told me that he examined the patient he reported on in 1916 a few days ago. At the time of the report she was 8 years of age. She has remained well throughout this period, and no new lesions have developed. The depressions at the site of former lesions have remained.

ACANTHOSIS NIGRICANS

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MEDICAL CORPS, ARMY OF THE UNITED STATES

Since the original reports of acanthosis nigricans by Pollitzer [1] and Janovsky,[2] about 300 authentic cases have been described. These included instances both of the juvenile and of the malignant type of the disease. In reviewing the literature, it was noted that in the majority of the cases the disease was associated with a malignant growth in the abdomen.

The consensus is that in many cases acanthosis nigricans is due to the presence of tumors adjacent to the abdominal sympathetic system and adrenal glands. Wieder [3] concluded that in many cases, including cases of the juvenile type, the disease cannot be accounted for by this hypothesis. Many investigators have described cases of acanthosis nigricans associated with some systemic maligant growth, usually involving the stomach or uterus. Many of the patients have been infants and children. Usually the younger the patient the more unlikely the association of a malignant growth. Yet this circumstance does not mean that the age alone may be used in determining the presence or the absence of a neoplasm. Long observation and the absence of cancer may be used in making a distinction of types. Usually when acanthosis nigricans occurs in an adult 40 years of age or over, it is quickly followed by evidence of a malignant condition. If acanthosis nigricans follows a malignant growth it presages a fulminating course. Reviewing the analysis of Mukai's statistics,[4] Masson and Montgomery [5] indicated the probable percentage of cancer in various age groups.

From Lawson General Hospital, Brig. Gen. W. L. Sheep commanding and Col. E. E. Cooley chief of medical service.

Released for publication by the War Department Manuscript Board, which assumes no responsibility, other than censorship, for the contents of the article.

1. Pollitzer, in Unna, P. G.; Morris, M.; Duhring, L. A., and Leloir, H.: Internationaler Atlas von seltenen Hautkrankheiten, Leipzig, Leopold Voss, 1890, plate X.

2. Janovsky, in Unna, P. G.; Morris, M.; Duhring, L. A., and Leloir, H.: Internationaler Atlas von seltenen Hautkrankheiten, Leipzig, Leopold Voss, 1890, plate XI.

3. Wieder, L. M.: Acanthosis Nigricans: Juvenile Type, J. A. M. A. **87:** 1964 (Dec. 11) 1926.

4. Mukai, T.: Acanthosis Nigricans, Acta dermat. **14:**460, 1929.

5. Masson, J. C., and Montgomery, H.: Relationship of Acanthosis Nigricans to Abdominal Malignancy, Am. J. Obst. & Gynec. **32:**717 (Oct.) 1936.

Many theories for the benign type of acanthosis have been advanced, such as changes in temperature,[6] alcoholism, decapsulation of the kidneys [7] and syphilis.[8] Grace and Schwartz [9] were unable to show any malignant growth or definite involvement of the endocrine system in their case. The endocrine features and the possible association of nevi and cancer were reviewed by Curth.[10] From the family histories of patients with acanthosis nigricans and the association of acanthosis nigricans with cancer in the same patient, she concluded that there is a genetic relationship between the two conditions. The exact mechanism of this is still unknown. Recently I encountered a patient suffering from acanthosis nigricans associated with severe urticaria.

REPORT OF A CASE

History.—M. R., an unmarried American soldier, aged 29, was seen in September 1941 for the first time. He was admitted to the hospital for treatment of an eruption, first noticed by him in July 1941. Since that time he has not been free from it for any period. The only subjective symptoms were pruritus and burning of the skin, which became more severe in warm temperature.

The patient stated that he was well until he was given injections of tetanus toxoid early in July 1941. Immediately after receiving the first injection he noticed an intense itching throughout the body. Later he was given two more injections, which made his condition much worse. This was followed by an erythematous and urticarial eruption, which disappeared in a short time. After the disappearance of the acute erythema he began to notice changes in the color of his skin. According to the patient, the eruption began first in the axillas and rapidly spread to the neck. About one month later he noticed that his perineum was also involved. The soldier was hospitalized at Station Hospital, Dale Mabry Field, Tallahassee, Fla. He was treated with many topical preparations, some of which gave palliative relief. He found that crude coal tar, 3 per cent, reduced the discomfort but did not alter the progress of the eruption. The condition has persisted for five months.

The soldier had the usual diseases of childhood without complications. Tonsillectomy was performed in 1934 and appendectomy in 1935. At birth he presented a pigmented lesion on the left side of the abdomen, which has become neither larger nor darker.

Family History.—The maternal grandmother died at the age of 85, of an unknown cause. The paternal grandmother died at the age of 50, of tuberculosis of the throat. The father, who was killed in an accident at the age of 49, had

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6. Crocker, H. R.: Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., 1908, p. 597.

7. Wise, F.: Acanthosis Nigricans, J. Cutan. Dis. **36**:35 (Jan.) 1918.

8. Caussade, G.; Lévy-Franckel, A., and Juster: Acanthosis Nigricans, Bull. et mém. Soc. méd. d. hôp. de Paris **46**:1363 (Oct. 20) 1922.

9. Grace, A. W., and Schwartz, H. J.: Acanthosis Nigricans, Arch. Dermat. & Syph. **29**:691 (May) 1934.

10. Curth, H. O.: Benign Type of Acanthosis Nigricans, Arch. Dermat. & Syph. **34**:353 (Sept.) 1936.

been physically normal before his death. The mother, 52 years old, was in good health. Three brothers and three sisters, varying in age from 15 to 34, were apparently sound. There was no history of any eruption in the family.

Physical Examination.—At the time of examination the patient did not appear acutely sick and was ambulatory. He had lost some weight but did not appear ill nourished. The pupils were normal and reacted to light and in accommodation. Examination of the anterior segments of both eyeballs revealed no abnormalities. The right disk and fundus appeared perfectly normal. On the margin of the left disk, between 7 and 8 o'clock, there was an oval dirty gray area about 5 by 10 mm. in size perpendicular to the margin of the disk. The pharynx and teeth were normal. There was no cervical lymphadenopathy. Examination of the lungs and heart showed nothing abnormal. The blood pressure was 128 mm. of mercury systolic and 68 mm. diastolic. There was no tenderness or palpable mass in the abdomen. A complete neurologic examination disclosed no pathologic signs.

Laboratory Examination.—Examination of the urine revealed no albumin or sugar. The Kahn and Wassermann reactions were negative. The results of the examination of the blood were as follows: hemoglobin, 90 per cent; red cells, 5,280,000; white cells, 8,900, with polymorphonuclear leukocytes 48 per cent, lymphocytes 49 per cent, eosinophils 1 per cent and mononuclear leukocytes 2 per cent; urea nitrogen 15 mg., chlorides (blood) 429 mg. and sugar 77 mg., per hundred cubic centimeters. The basal metabolic rate was +2 per cent. The gastric analysis showed 23 degrees of free hydrochloric acid. Gastroscopy showed atrophic gastritis.

Roentgen Examination.—The sinuses were normal. On examination of the chest, the hilar shadows were accentuated with scattered foci of calcifications. There was no calcification in the area of the adrenal glands. The esophagus, stomach and duodenum were normal. A roentgenogram of the skull showed no evidence of intracranial pathologic change except some calcification of the pineal gland; this density was in the midline without displacement.

Cutaneous Tests.—Cutaneous tests showed no strongly positive reaction to anything save tetanus toxoid; a 1:10 dilution of this antigen elicited a strong reaction.

Exploratory Laparotomy.—Exploratory laparotomy did not show any evidence of malignancy.

Examination of the Skin.—Clinical: The changes in the skin were symmetric with the exception of the unilateral nevi on the left side of the abdomen. The eruption involved the neck, axillas, forearms, abdomen, nipples and perineal regions. The neck was wholly involved, and the eruption was bandlike, darker than normal skin with an exaggeration of the normal folds. Both axillas were uniformly involved. The eruption was well circumscribed and consisted of discrete and confluent lesions with irregular borders. The involved areas showed some discoloration and the formation of deep furrows in the lines of cleavage. The natural lines of the skin were exaggerated with definite papillary hypertrophy. The exaggerated folds were more pigmented. In places mild papillomatous growths were noticed. About the eye, on the lower lid, there was a small warty nevus. The nipples were both involved and showed darkly pigmented and hypertrophic skin with accentuation of the normal furrows. There was complete loss of hair about the nipples. Both arms, especially the forearms, were involved; many soft, slightly pigmented, warty growths, varying in size from that of a millet seed to that of a pea, were noticed here. On the upper part of the back, bridge of the nose and upper part of the chest there were a number of pigmented nevi. The perineum showed practically the same

lesions as the axillas. The nails showed no change; the tongue was rough and slightly darkened. To touch, the skin was dry. He also had recurrent generalized evanescent wheals (of six months' duration).

Histologic (Major E. T. Thorsness): The section of skin under low power magnification revealed moderate loose hyperkeratosis, acanthosis, subepithelial edema and hypertrophy of the granular layer and papillary bodies, producing a wavy cuticular surface. High power magnification revealed moderate spongiosis and subepithelial infiltration of lymphocytic cells and also a slight increase in subepithelial chromatophores.

A section of skin taken from a growth in the right axilla revealed a benign subcutaneous nevus.

A section of skin taken from the pigmented area which has been present since birth showed an epidermal nevus.

COMMENT

There was no sign or symptom that indicated a definite etiologic agent in this case, but there was a definite clue to a contributing factor. It is interesting to note that the eruption was noticed shortly after injections of tetanus toxoid. Dr. Fred Wise, in the discussion of Wieder's case,[3] told of a reaction in a hysterical woman following decapsulation of the kidneys. In his case the inflammatory reaction was followed by the typical picture of acanthosis nigricans. This sequence of events may be assumed to be coincidental, as it is most difficult to see the relationship of the injection of a foreign protein. Yet the initial erythematous and urticarial eruption may have been sufficient to touch off the mechanism by which the acanthotic process followed. Can it be assumed that the disease developed on a basis of constitutional hypoadrenalism, as the result of some exogenous noxa? Is it necessary that the adrenal glands be grossly involved, or can microscopic changes bring about the manifestation of insufficiency or dysfunction? Need both adrenal glands be diseased to produce symptoms, or is the sound side affected reflexly? This patient had a low blood sugar value, easy fatigability and urticaria. May this indicate insufficiency of chromaffin? There is a direct relationship between the sympathetic nerves and the chromaffin system. The sympathetic nerves are believed to act as inhibitors of pigmentation; their paralysis could lead to hyperpigmentation. Could the injected tetanus toxoid be the exogenous noxa that unbalanced the endocrine influence so as to cause dysfunction of the sympathetic nerves and produce the syndrome recognized as acanthosis nigricans? If that is assumed to be the case, it and other similar benign causes could explain the benign type of acanthosis nigricans. This is most hypothetic.

Clinically and histologically the cutaneous lesions are similar in both the juvenile and the malignant type of this disease. This may not indicate that the same causative factors are present. In other words, the clinical eruption may be identical or practically so without having the

same instigation factors. It must be assumed until further evidence can be presented that the etiologic factors in both types of the so-called acanthosis nigricans are unknown. In the case presented at this time at least there is present some evidence of endocrine dysfunction.

The other interesting findings are the lesion in the left eye and the severe urticaria. Whether the lesion in the eye is a developmental defect or a new growth could not be determined. The urticarial eruption has been severe, consisting sometimes of erythema-multiforme-like lesions. The usual forms of treatment, including elimination diets, epinephrine, liver extract, calcium and autohemotherapy, have been of little value.

SUMMARY

A case of acanthosis nigricans associated with urticaria is reported. The clinical and histologic pictures are presented. A brief review of some of the interesting cases is given. The possible role of injections of tetanus toxoid as a causative agent of the acanthosis nigricans is considered.

Clinical Notes

AN UNUSUAL CASE OF MATCH DERMATITIS

ABRAHAM FISHER, M.D., McKEESPORT, PA.

J. A., a white man aged 32, presented an acute erythematous eruption involving the entire width of the lower part of the forehead, including the eyebrows, a patch on the left side of the neck, one on the left side of the chest and one on the lower right side of the abdomen. The dermatitis had begun on his forehead seven months prior to my examination. The neck was involved later and then the chest and the abdomen during the summer months, when he did not wear an undershirt. During this seven month period he had several acute exacerbations and remissions.

Questioning revealed that the patient used ordinary kitchen matches and that he scraped his right thumb nail against the head of the match to ignite it. During working hours, when he was confined to a small room, he became warm and perspired freely. He would then wipe his right thumb nail across his forehead and the left side of his neck. He kept his matches in either his shirt pocket or the watch pocket of his trousers, and during the warm months, when he wore no undershirt, the adjacent areas of his skin became involved.

The reaction to a patch test with the head of a match was strongly positive. Tests with the same type of match applied to 6 other persons as controls elicited no reaction.

After the patient discontinued the use of this type of match, the eruption cleared completely and did not recur.

530½ Fifth Avenue.

PSORIASIS IN A FULL-BLOODED NEGRO

Report of a Case

ARTHUR SAYER, M.D., NEW YORK

Psoriasis is a rather common dermatosis among Caucasians, but it is a rarity among Negroes. Only a few instances of psoriasis in full-blooded Negroes have been recorded in the American literature, by Dade,[1] Fox,[2] Parounagian [3] and Wright.[4] A search of the American literature of the past fifteen years has failed to reveal any additional reports of psoriasis in a full-blooded Negro.

From the Dermatology Department of the Morrisania City Hospital.

1. Dade, L. A.: Psoriasis in a Negro, J. Cutan. Dis. **27**:207 (Jan.) 1909.

2. Fox, H.: Psoriasis in a Full Blooded Negro, J. Cutan. Dis. **34**:847 (April) 1916.

3. Parounagian, M. B.: Psoriasis in a Full Blooded Negro, Arch. Dermat. & Syph. **13**:106 (Jan.) 1926.

4. Wright, C. S.: Psoriasis in a Negro, Arch. Dermat. & Syph. **9**:398 (March) 1924.

REPORT OF CASE

H. S., a full-blooded Negro aged 51, a laborer, born in Virginia, came to the dermatologic clinic of Morrisania City Hospital on Aug. 16, 1941. He presented an extensive eruption which had been present for over twenty years and for which he had never previously consulted any physician. The major portion of the eruption

Psoriasis in a full-blooded Negro.

was situated on the buttocks, lower extremities and forearms. It was present to a much less extent on the scalp, neck and trunk. The eruption consisted of guttate and nummular lesions and larger plaques of various sizes and shapes. The lesions on the buttocks and lower extremities were mainly confluent, while on the rest of the body they were mainly discrete. The lesions were dry, moderately elevated, nonpruritic and covered with silvery scales, which were readily removed by scraping. There were many bleeding puncta after removal of the scales. The eruption therefore had all the clinical characteristics of psoriasis.

The clinical diagnosis was confirmed by a biopsy of one lesion on the right buttock. The Wassermann reaction of the blood was negative. The urine and a blood count were essentially normal.

COMMENT

Because psoriasis is not so rare in Negroes who have an admixture of white blood, I have tried to establish the fact that my patient was a full-blooded Negro. He stated that both of his parents and all of his grandparents (whom he distinctly remembers) were very dark skinned, and he felt certain that they were full-blooded Negroes. He also stated that all of his brothers and sisters were dark skinned and had the same color as his own. The patient had all of the known external negroid facial characteristics. His skin was black, and his hair was black and kinky. His nose was short and turned up, the tip was broad and the cartilage of the tip was single and not split in the midline. On the basis of the aforementioned statements, I feel that there is ample evidence that this man was a full-blooded Negro.

145 Central Park West.

Obituaries

EDWARD ROBERT MALONEY, M.D.
1875-1942

In the sudden and unexpected death of Dr. Edward R. Maloney on Oct. 5, 1942, American dermatologists have lost a most useful and generally beloved member. Dr. Maloney was born on Feb. 6, 1875, in Norwich, Conn., the son of William Maloney, a merchant, and Mrs. Julia Grafton Maloney. His premedical education was obtained at the Norwich Academy, and in 1896 he received the degree of Doctor of Medicine at the College of Physicians and Surgeons, Columbia University, New York.

Dr. Maloney interned at St. Vincent's Hospital in New York, an institution in which he was always greatly interested and which he served with distinction as president of the medical board during the last six years of his life. He began the practice of medicine in 1899 in the city of New York, where he spent the remainder of his life.

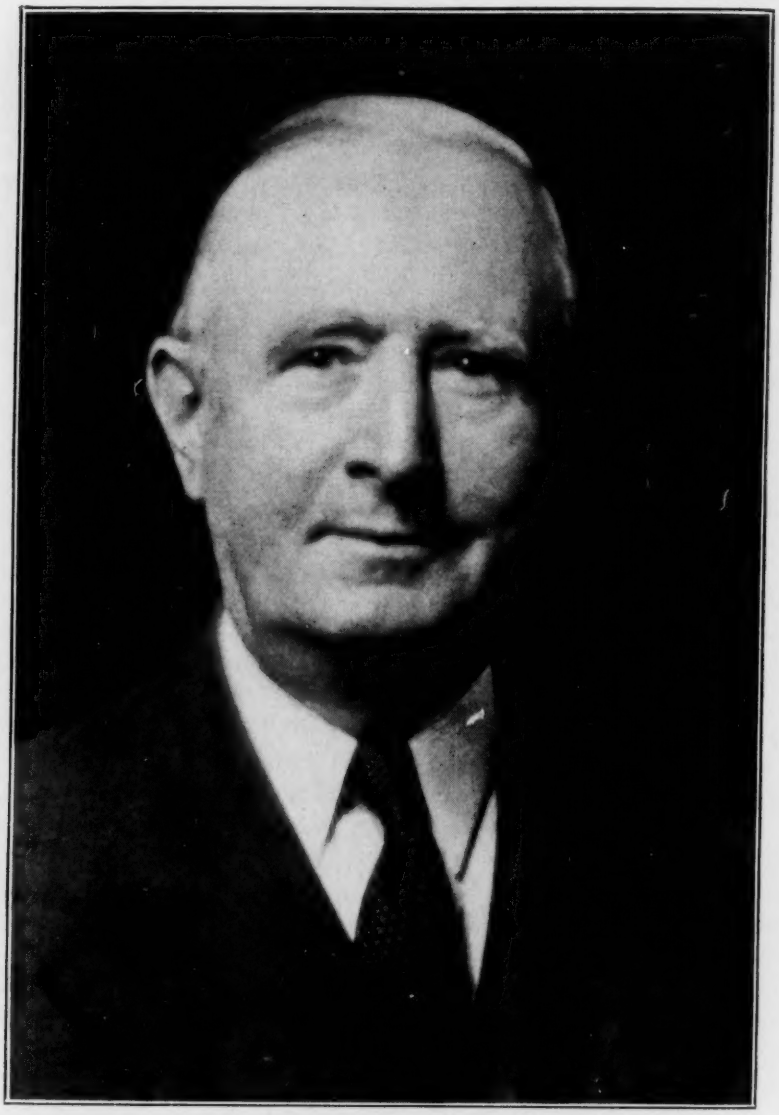
Dr. Maloney was a type of dermatologist of whom there are few at the present day, who spent the first twenty years of his medical career in general practice. He served for years as a diagnostician in the department of health of New York city, and from 1910 to 1912 he was assistant professor of pulmonary diseases at Fordham University. From 1905 to 1909, he was clinical assistant in surgery at the New York Post-Graduate Hospital.

Dr. Maloney's interest in dermatology began in 1919, when he was appointed clinical assistant at the New York Skin and Cancer Hospital (where he served for three years) and attending dermatologist to the dispensary of the University and Bellevue Hospital Medical College (as it was then called). At the latter institution, in 1925 he was appointed chief of clinic. He soon showed unusual talent for administrative work and became an invaluable member of the staff. The progress that was made under considerable difficulties in changing from a comparatively small service to a large and active one was due largely to the administrative genius and tactful ways of Dr. Maloney. He was eventually appointed associate professor at the New York University College of Medicine (the new name of the institution) and attending dermatologist and syphilologist to Bellevue Hospital.

In 1938 Dr. Maloney became head of these services, being retired at the end of two years for age, according to the rules of the university. He was then made professor emeritus at the university and honorary consulting dermatologist and syphilologist at Bellevue Hospital.

Dr. Maloney's ability as a dermatologist was shown by the numerous honors he received. He was elected a member of the New York Der-

matological Society in 1926, serving as its president in 1940-1941. He became a member of the American Dermatological Association in 1928 and served as chairman of the section on dermatology and syphilology



EDWARD ROBERT MALONEY, M.D.
1875–1942

of the Medical Society of the State of New York in 1932. He was a member of the American Academy of Dermatology and Syphilology and a specialist certified by the American Board of Dermatology and Syphilology (Founder's Group). His interest in the New York Acad-

emy of Medicine was rewarded by his election as chairman of the Section of Dermatology and Syphilology in 1927-1928 and as chairman of the committee on admission of the Academy in 1941. He was also a member of the Celtic Society, serving as its president in 1930-1931.

The institutions with which he was connected at the time of his death as attending or consulting dermatologist included Bellevue and St. Vincent's hospitals, New York Infirmary for Women and Children and New York Foundling Hospital, New York; Elizabeth A. Horton Memorial Hospital, Middletown, N. Y., and Pilgrim State Hospital, Brentwood, N. J.

Dr. Maloney was not a prolific writer, but his publications were always carefully constructed and well written. They exemplified his good common sense and, above all, his scientific honesty.

There are few, if any, dermatologists who have had a longer and more distinguished military record than Colonel Maloney. He was commissioned captain, medical corps, in the New York National Guard in 1907 and was assigned to the Ninth Regiment. He was promoted to the rank of major in 1921. He served as a member of the examining board for Coast Artillery officers from 1912 to 1914 and on a similar board for medical officers from 1914 to 1917. He was assigned to the division staff of the sixth division in 1915 and became acting division surgeon during the Mexican border service in 1916-1917. He was promoted to the rank of lieutenant colonel in 1917 and appointed division surgeon of the twenty-seventh division. He organized the medical department of this division and commanded it during the greater part of the war, serving both in the United States and in Belgium. After the war he was commissioned colonel in the medical reserve corps.

Colonel Maloney was a natural-born soldier. He understood the value of discipline and loyalty and, above all, justice in his relations with others in the military service. His interest in military affairs was exceeded only by his devotion to his wife and his profession.

Dr. Maloney was a strong character and one who would fight for a principle. He was able to make definite and, if necessary, quick decisions, a quality which was invaluable in his military as well as in his civil career. His guiding principle was to be fair and just at all times in dealing with his fellow men. He had a delightful personality and made a host of friends, by whom he will be sorely missed.

A final tribute to his memory was paid at a solemn requiem mass at the chapel of St. Vincent's Hospital. Archbishop Spellman presided, and other high dignitaries of the Catholic church were present. A military guard of honor was present, and taps were blown at the conclusion of the service. The burial took place in the Arlington National Cemetery.

Dr. Maloney is survived by a widow, Mrs. Lilian H. Maloney, and by one brother and two sisters.

HOWARD FOX, M.D.

DAVID KING SMITH, M.D.

1873–1942

David King Smith, M.B., F.R.C.P. (Can.), died suddenly on Nov. 3, 1942, at his home in Toronto, Canada, as the result of cerebral hemorrhage.

Born in Toronto in 1873, he was the son of Dr. Andrew Smith and Mrs. Mary Smith. He received his education at the Model School, Jarvis Collegiate and the Medical School of the University of Toronto, graduating in 1896. He then proceeded to postgraduate work in London, England, and later in the United States. He soon showed an interest in diseases of the skin and became attached to the clinic for diseases of the skin at the Toronto General Hospital. In 1912 he became head of the department, a position which he held until 1928.

For many years Dr. Smith served as medical officer with the Forty-Eighth Highlanders, and during the great war he served with No. 4 Canadian General Hospital in England and in Salonika. He was invalided home with a malignant type of malaria, but, such was his courage, he was soon found on duty again as officer in charge of the Military Hospital at Halifax, Nova Scotia, rendering great service at the time of the Halifax disaster. Later he was officer commanding the Davisville Convalescent Hospital for returned soldiers.

Dr. Smith retired from the army at the close of the war with the rank of colonel and became consultant in diseases of the skin at Christie Street Hospital for returned soldiers.

Dr. Smith was always interested in general medicine and was elected president of the Toronto Academy of Medicine in 1930. He was a member of the British Association of Dermatology and Syphilology (Canadian Branch), the American Dermatological Association and many other associations of a scientific nature. He was a member of the Zeta Psi fraternity, the York Club, St. Andrew's Society, the Toronto Hunt Club and the British Empire Club of London, England.

Dr. Smith was a man of strong principles and honor. He was always cheerful and friendly and endeared himself to a wide circle of staunch friends wherever he went. He was always interested in sports, and during his university and school career he took part in most of the athletic activities; he was especially good in track and field events and at one time held the all round university championship. A great lover of horses, he followed the hunt for many years, until his health no longer permitted.

Dr. Smith's contributions to medical literature were not many, but the articles he wrote, though brief, were to the point and always practical. Canadian dermatology has lost one of its oldest and staunchest supporters.

Dr. Smith is survived by his wife, a daughter, Mrs. Graham Cassels, and a son, Andrew.

E. J. Trow, M.D.

News and Comment

THE ROLE OF THE PHARMACIST IN CONTROLLING VENEREAL DISEASES

Pharmacists are playing an important role in the wartime control of venereal diseases, the American Hygiene Association announced in making available to the medical profession a report based on a recently completed survey.

Drugstore counter prescribing for syphilis and gonorrhea has greatly decreased, the association reports. Forty-six cities in fifteen states were visited and 716 drugstores studied. Only 11 per cent of the drugstores visited offered diagnosis and treatment for conditions presumed to be syphilis and gonorrhea. Thirty-two per cent sold remedies on specific request but did not attempt to diagnose, and 57 per cent urged immediate and well qualified medical care. In a large proportion of the drugstores where remedies are stocked and sold, the druggist advised that "self medication is bad and dangerous business."

DEATHS

Dr. Frank W. Cregor died on Dec. 9, 1942, at Indianapolis.

Correspondence

SCLERIASIS (SCLEREDEMA ADULTORUM) AS FIRST DESCRIBED BY PIFFARD

To the Editor:—Recently I acquired a copy of Henry G. Piffard's "An Elementary Treatise on Diseases of the Skin, for the Use of Students and Practitioners" (New York, Macmillan & Co., 1876). Concerning this remarkable volume I quote from Bechet's article in the ARCHIVES (**45**:482 [March] 1942), "The Early History of American Dermatology": "In 1876 Piffard published his book, the second textbook on diseases of the skin published in America and by no means elementary, as the modest title suggested. It was a masterly treatise, giving a complete summation of the dermatologic views up to that time interspersed with Piffard's own valuable opinions."

The appropriateness of these remarks can readily be confirmed by the following illustration of Piffard's keen powers of observation. Chapter 39 of his treatise is headed "Scleroderma—Scleriasis." In the opening paragraph the author expresses the opinion that among the large number of reported cases of a condition characterized by "Hardness and inelasticity of the integument . . . two distinct affections have been confounded under the same, or similar names . . . . In one of these diseases the lesion is exceedingly chronic, and spreads from one or more points in patches or bands. It may occupy years in its progress, and is uninfluenced by the usual therapeutic agencies. It exhibits well-marked pathological changes. In the other affection the invasion is rapid, and the lesion extensive, the whole of the upper part of the body becoming involved in a few weeks or even a few days. Recovery may take place under the most varied treatment, or even spontaneously. Under the microscope, sections of the skin present a normal aspect."

Piffard then proceeded to describe, first, a typical example of progressive scleroderma and, secondly, an example of a different condition, to which he gave a somewhat similar title, namely, scleriasis.

The latter disease occurred in a blacksmith aged 49 who suffered from emphysema and bronchitis. In March of 1870 he noticed a stiffness of the neck, which was soon followed by a similar condition of the arms, back, chest and abdomen. The disease reached its height in ten days, remained stationary for about four weeks and then began slowly to decline. The skin was adherent to the underlying parts but not discolored. It was impossible to lift the skin or pick it into folds. There was no pain, but the patient complained of a sense of inconvenience, as from being encased in an inelastic covering which impeded his movements. Otherwise his organs seemed in normal condition.

In discussing this case of scleriasis Piffard stated: "The peculiarities of this case as distinguished from the one previously recited, are its rapid invasion of a large portion of the surface, its apparent spontaneous recovery, and the absence of appreciable histological change. These would seem to me to be sufficient to warrant its consideration as a separate affection, and as such entitled to a different name. Many of the cases of scleroderma heretofore reported have been of this description, and should have been earlier recognized as essentially differing from the chronic, almost incurable, and sometimes fatal disease to which alone I would confine the name of scleroderma. . . . The etiology of this affection is as obscure as

that of true scleroderma. . . . Scleriasis, in the majority of cases that are recorded, seems to tend toward a spontaneous recovery. This may be doubtless facilitated by baths, frictions, massage, and the like; but it is doubtful if there are any internal remedies which have any special influence upon the course of the affection."

There is, of course, not the slightest reason to doubt that Piffard has here published the first account of the entity which Buschke was to describe over thirty years later as scleredema adultorum and subsequent writers as scleredema. Here is a classic instance of the neglect by later writers of a clearcut description of a hitherto undescribed disease, with the common sequel of the republication of its description at a later date under another name.

It is a satisfaction to point out that scleredema was first accurately described and differentiated from scleroderma by one of the pioneers of American dermatology.

M. H. Saffron, Major, M. C., U. S. A.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

THE EARLY DIAGNOSIS OF SYPHILITIC AORTITIS. S. BOHARAS, LESTER HOLLANDER and MAURICE GOLDSMITH, Am. J. M. Sc. **203**:54 (Jan.) 1942.

Because of the poor results of treatment when syphilitic aortitis is unrecognized until after the development of complications (regurgitation, aneurysm or coronary stenosis), Boharas, Hollander and Goldsmith attempted to determine the feasibility of early diagnosis of uncomplicated aortitis. Two hundred syphilitic persons were studied clinically, roentgenologically and by electrocardiogram. The aortic arch and root were measured by three methods. Two hundred nonsyphilitic persons of the same age were studied as a control group.

The authors conclude that a positive clinical diagnosis of early syphilitic aortitis is practically impossible. The electrocardiographic changes of cardiovascular syphilis develop late in the disease and are relatively unimportant clinically. There are no physical signs that are pathognomonic of this condition, although the tympanitic aortic second sound may be of some value in diagnosis.

Roentgen study allows recognition of local aortic dilatation, but this sign is not pathognomonic of syphilitic aortitis. Diffuse dilatation is a reliable sign, but one must rule out hypertension, arteriosclerosis and rheumatic aortic insufficiency. Transverse measurements of the root of the aorta have relatively little worth in individual cases, although average values in groups of cases show increased width in more of the patients with syphilis.

STUDIES OF THE B VITAMINS IN THE HUMAN SUBJECT. THOMAS E. MACHELLA, Am. J. M. Sc. **203**:114 (Jan.) 1942.

Of 17 patients with cheilosis, Machella reported that all had been on an inadequate diet and 15 presented additional evidence of deficiency of vitamin B complex. In 12 of the patients the eruption was limited to the angles of the mouth. On administration of riboflavin 8 showed no improvement. There were some favorable responses to the use of pyridoxine and of nicotinic acid. Three patients with bleeding lesions did not improve until ascorbic acid was given.

SYPHILITIC AORTIC INSUFFICIENCY: THE ASYMPTOMATIC PHASE. WALSH MCDERMOTT, RALPH R. TOMPSETT and BRUCE WEBSTER, Am. J. M. Sc. **203**:202 (Feb.) 1942.

In spite of the generally accepted attitude of discouragement with the outlook in syphilitic aortitis, the authors recall Grant's reported statistics (1933) showing a mortality rate of only 64 per cent ten years after the original examination. McDermott, Tompsett and Webster reviewed the records of 91 patients having syphilitic aortitis with aneurysm in whose cases the diagnosis was based on the repeatedly demonstrable presence of a diastolic murmur over the aortic area or down the left sternal border, known syphilitic infection and no evidence of mitral stenosis or congenital heart disease either clinically or roentgenographically. Only 31 of these patients sought care because of symptoms referable to the heart. It is pointed out that aortic syphilis seen by most internists occurs in persons who have sought medical care because of symptoms of cardiac insufficiency. The authors suggest that aortic insufficiency due to syphilis is actually present in a clinically recognizable form for a relatively lengthy period of time before the development of symptoms and that the usual prognostic data are not applicable to this large group of patients.

Of 20 patients having no symptoms and observed for more than two years, symptoms developed in only 2. Of 8 patients who admitted having symptoms only after questioning subsequent to examination, 1 died three and one-half years after the diagnosis and the others were observed at least two years. Fifteen patients were followed more than two years after having had symptoms at the time of diagnosis; 6 of these died as a result of heart disease. Thus, 46 per cent of the entire group had been followed more than two years.

All of this group of 91 patients had definite serologic evidence of syphilis or a history of such evidence. One patient had a negative Wassermann reaction of the blood, but the reaction of the spinal fluid was positive. This was a selected group of patients; so the authors undertook a study of 44 others with aortitis admitted to the wards without knowledge of the presence of syphilis. In 32 the reaction was positive; in 6 it was doubtful but had previously been positive, and 1 had an anticomplementary Wassermann reaction of the blood serum but the Wassermann reaction of the spinal fluid was positive. With the blood of 2 patients a doubtful reaction was obtained, and for 3 others the only evidence was a 1 plus to 3 plus Kline reaction.

EFFECT OF ESTROGEN ON THE UTILIZATION OF THE VITAMIN B COMPLEX. JOHN ASHWORTH and DON C. SUTTON, Arch. Int. Med. **69**:15 (Jan.) 1942.

In reporting observations on a series of 7 cases the authors point out that the administration of an estrogen to a person with a subclinical deficiency of vitamin B complex may cause the appearance of lesions characteristic of (*a*) thiamine deficiency (polyneuritis), (*b*) nicotinic acid deficiency (pellagra) or (*c*) riboflavin deficiency (cheilosis). It was thought that the estrogens either increase the demand for or suppress the utilization of the vitamin B complex. Since the patients reported on in this paper gave evidence of vitamin B deficiency before therapy was begun, Ashworth and Sutton state that their observations should not be interpreted as a contraindication to the usual therapeutic uses of estrogens.

DESTRUCTIVE OSSEOUS LESIONS IN EARLY SYPHILIS. F. W. REYNOLDS and H. WASSERMAN, Arch. Int. Med. **69**:263 (Feb.) 1942.

In the records of a series of 10,000 cases of early syphilis Reynolds and Wasserman found that destructive osseous lesions had been recognized in only 15 instances. They state that early osseous syphilis must be differentiated most frequently from pyogenic osteomyelitis, tuberculous osteitis and multiple myeloma. Pain and localized tumefaction are the cardinal symptoms of destructive osseous lesions. The most frequently associated disease is arthritis. Response to treatment is favorable.

The fundamental process is one of osteolysis with replacement by syphilitic granulation tissue. In roentgenograms the lesions of the skull are characteristic, consisting of irregularly circular areas of decreased density having a moth-eaten appearance; elsewhere the bony changes are less diagnostic, although involvement about the sternoclavicular joint is suggestive.

HAMARTIAL NATURE OF THE TUBEROUS SCLEROSIS COMPLEX AND ITS BEARING ON THE TUMOR PROBLEM. SYLVAN E. MOOLTEN, Arch. Int. Med. **69**:589 (April) 1942.

Moolten reports a case of the tuberous sclerosis complex in which the disease was first brought to light clinically by hemorrhage from a renal hamartoma. He states that more than half the patients with this complex have renal tuberosities which are generally latent clinically. A review of their pathologic changes shows that they are better classified as hamartomas than as neoplasms.

Cutaneous lesions (adenoma sebaceum) are estimated to be present in half the cases of tuberous sclerosis. Most dermatologists are familiar with this association,

but not all realize that there is a considerably heightened incidence of cerebral neoplasm in these patients. Rhabdomyomas of the heart are also met with frequently. Moolten also mentions some pathognomonic retinal tumor-like lesions known as phacoma. Osseous lesions are not common and are similar to those observed in association with multiple neurofibromatosis.

This concept of a more generalized nature of the disease leads Moolten to suggest the use of the term disseminated hamartiosis (Bourneville type). There is a similarity to neurofibromatosis, and fragments of one complex are occasionally met with in the other. Each also has some features of resemblance to Lindau's disease (angiomatosis of the retina and central nervous system), Osler's disease (hereditary angiomatosis) and congenital polycystic disease. Thus the tuberous sclerosis complex should be regarded as a widespread developmental anomaly, often hereditary, in which the primary abnormality lies in the faulty differentiation of tissues rather than organic body units, though the brain, skin, heart, kidneys, retina and bones are most frequently involved.

ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS WITHOUT CUTANEOUS MANIFESTATIONS AND WITH HERETOFORE UNDESCRIBED PULMONARY LESIONS. HAROLD L. RAKOV and J. SPOTTISWOOD TAYLOR, Arch. Int. Med. **70**:88 (July) 1942.

Rakov and Taylor report extensive microscopic studies of pulmonary changes observed in a case in which they made a diagnosis of acute disseminated lupus erythematosus, though at no time were cutaneous lesions observed. The most prominent clinical signs were those of consolidation of the lungs, persisting from early in the course of the disease until death eight months later. At necropsy the lungs were small and atelectatic and the pleural spaces were obliterated by easily separated adhesions. Microscopically, lobular consolidation was apparent and the alveolar septums presented low grade chronic inflammation with the cells almost entirely mononuclear.

The authors admit the difficulty in establishing a diagnosis of lupus erythematosus in the absence of cutaneous lesions, but in this case the other clinical and pathologic features pointed strongly to this disease.

LYNCH, St. Paul.

THIAMINE HYDROCHLORIDE IN THE TREATMENT OF TRYPARSAMIDE AMBLYOPIA. P. J. LEINFELDER and R. B. STUMP, Arch. Ophth. **26**:613 (Oct.) 1941.

The subject of tryparsamide amblyopia is a serious one to the neurologist, and any means of combating the condition must be seriously considered.

In 1939 Muncy reported 50 cases in which vitamin B_1 and vitamin B complex were administered during the course of tryparsamide therapy, and from his study of these cases he gained the impression that yeast tablets are protective against tryparsamide amblyopia. He also reported a case in which preexisting tryparsamide amblyopia was improved after administration of yeast tablets.

To test this assumption, Leinfelder and Stump injected thiamine hydrochloride intramuscularly in large doses into patients who showed changes in the visual fields after administration of tryparsamide. They report the cases of 2 of these patients.

The authors conclude that the use of thiamine hydrochloride was of no value in the treatment of changes in the visual fields occurring as a result of tryparsamide therapy. Although both patients received large doses of the vitamin, the visual fields continued to undergo progressive contraction.

SPAETH, Philadelphia [ARCH. NEUROL. & PSYCHIAT.].

RELIABILITY AND SIGNIFICANCE OF THE GORDON TEST IN HODGKIN'S DISEASE. PAUL E. STEINER, Arch. Path. **31**:1 (Jan.) 1941.

In 1932 Gordon described a syndrome in rabbits and guinea pigs receiving intracerebral injections of a broth suspension of lymphogranulomatous tissue. It consisted of spastic paralysis, incoordination and ataxia, retraction of the head, fits and loss of weight. The author presents a study of the reliability and significance of the test.

In 21 cases of histologically proved Hodgkin's disease the reaction was positive in 16 and negative in 5. No positive results were obtained in 40 control tissues, including lymphosarcoma, pseudoleukemia, leukemia, nonspecific lymphadenitis and tuberculous lymphadenitis. Of 310 cases previously reported in the literature, in 73.9 per cent the reaction was positive, whereas in 452 control cases collected from the literature there was a positive reaction in 1.77 per cent. Most positive reactions in controls were observed in cases in which the lesions were easily differentiated microscopically.

The anatomic basis for the symptom complex produced in animals lies in degenerative changes in the Purkinje cells of the cerebellum. The agent producing this reaction has been found in human leukocytes, leukocytic cream from eosinophilic blood, myelocytic leukemia blood cream, normal human bone marrow, normal human spleen and other normal and pathologic tissues, as well as in the lymph nodes of patients with Hodgkin's disease. Its properties are those of a nonliving agent. The Gordon test is nonspecific, but it is reliable in differential diagnosis of diseases of lymph nodes if it is accompanied by histologic examination.

SHERMAN, Chicago [AM. J. DIS. CHILD.].

THE ROLE OF BASES IN OINTMENTS USED FOR PROTECTION AGAINST SUNLIGHT. ERNEST A. STRAKOSCH, J. Invest. Dermat. **5**:1 (Feb.) 1942.

The action of a light-absorbing chemical is dependent to a large degree on the ointment base in which it is incorporated. In the author's experiments petrolatum or hydrous wool fat afforded no protection against irradiation from an air-cooled quartz mercury vapor burner. A slight protective action was evident when an oxycholesterol-petrolatum ointment base or a base containing fatty acid esters of monoethanolamine mixed with petrolatum was applied. This action was enhanced when quinine or tannic acid was added to these bases, but the addition of quinine or tannic acid to petrolatum or hydrous wool fat did not increase the protection.

STUDIES WITH ANTIGENS: XII. PREPARATION AND PROPERTIES OF CONCENTRATES OF HOUSE DUST ALLERGEN. C. H. BOATNER and B. G. EFRON, J. Invest. Dermat. **5**:7 (Feb.) 1942.

The authors prepared an allergenically potent concentrate of house dust allergen by subjecting aqueous extracts of house dust to two successive fractional precipitations with dioxane, two successive precipitations from concentrated ammonium sulfate solution, and dialysis. The purified fraction is a dark brown glossy solid completely miscible with water. It exhibits the properties of both carbohydrates and proteins. The action of pepsin, of heat and of acid and base indicates that the house dust allergen is a stable substance of protein nature.

ELECTROPHORETIC SKIN STUDIES: I. REACTION TO COMMON GRASSES. HARRY H. SHILKRET, J. Invest. Dermat. **5**:11 (Feb.) 1942.

The author was able to produce by iontophoresis cutaneous reactions which were in general parallel with those elicited by the usual cutaneous tests (scratch and intradermal).

INDIVIDUAL ACTION AND SUMMATION EFFECTS OF X-RADIATION AND COMMONLY USED DERMATOLOGICAL PREPARATIONS ON THE SKIN OF THE ALBINO RABBIT. FRANK E. CORMIA and WILLIAM W. BRYAN, J. Invest. Dermat. **5**:15 (Feb.) 1942.

On the basis of the authors' experiments, which were made on the radioresistant skin of the rabbit, there appears to be no significant danger from the effect of most of the milder dermatologic preparations used in conjunction with

fractional roentgen radiation. Tar and other stimulating preparations should not be used in conjunction with roentgen radiation unless one desires to produce an extraordinary stimulation of an extremely chronic and thickened process.

FURTHER STUDIES IN ARSPHENAMINE HYPERSENSITIVENESS IN GUINEA PIGS: III. INVESTIGATIONS ON THE CHEMICAL SPECIFICITY OF SKIN HYPERSENSITIVENESS OF GUINEA PIGS TO OLD ARSPHENAMINE. WILHELM FREI, J. Invest. Dermat. **5**:29 (Feb.) 1942.

Intracutaneous testing of guinea pigs sensitized with old arsphenamine and of nonsensitized control animals gave the following results: The hypersensitiveness of the skin of the sensitized guinea pigs was not directed toward arsenic, toward the organic part of arsphenamine or exclusively toward arsphenamine, but it was directed in varying degree toward aromatic arsenicals in general.

EXPERIMENTAL BLASTOMYCOSIS IN MICE. JOSEPH M. HITCH, J. Invest. Dermat. **5**:41 (Feb.) 1942.

Studies on experimental blastomycosis in mice are presented, with determinations of the lethal dose of Blastomyces dermatitidis when given intraperitoneally. Protective or therapeutic effect of gentian violet on blastomycosis in mice was found to be nonexistent by all methods used. BLUEFARB, Chicago.

VITAMIN B AND E THERAPY IN TABES DORSALIS. SIMON STONE, J. Nerv. & Ment. Dis. **95**:156 (Feb.) 1942.

Stone points out that the treatment of tabes dorsalis has been less satisfactory than that of other forms of neurosyphilis. That this failure may be due to a neurotropic spirochete resistant to treatment is doubtful in view of the extreme rarity with which organisms have been demonstrated in the spinal cords of tabetic patients. In various food deficiency states, such as pellagra, alcoholism, diabetes and pernicious anemia, lesions resembling those of tabes have been observed in the posterior columns. In experimental animals similar lesions have been produced by diets deficient in vitamin B complex and vitamin E. Although dietary deficiency has not been demonstrated in cases of tabes, various authors have reported subjective improvement in tabetic patients with the use of thiamine hydrochloride and vitamin E.

Stone reports on the use of oral vitamin therapy (vegex, cod liver oil, liver extract, thiamine hydrochloride) in a group of tabetic patients receiving fever and arsenical treatment. The patients were better able to tolerate treatment. Since some patients failed to maintain the improvement noted, the intraspinal administration of thiamine hydrochloride was added to the other measures. Thirty to fifty milligrams of thiamine hydrochloride diluted in 5 cc. of fresh spinal fluid was injected slowly into the spinal canal at five to seven day intervals for one to five treatments. Improvement appeared in five to seven days, with reduction in the ataxia, urinary incontinence and frequency and severity of lightning pains. Improvement in visual acuity was observed. The intraspinal administration of thiamine hydrochloride as a safe and effective substitute for arsphenaminized serum is suggested.

Four patients without improvement under routine and fever therapy were treated with vitamin E. All showed improvement, especially when vitamin B complex was added. In general the improvement with intraspinal and combined therapy was greatest in patients with disturbances in gait, bladder difficulties and visual complaints. Gastric crises were reduced but not eliminated. Objectively, vibration sense reappeared in several cases.

Stone suggests that the lesions of tabes may be due to the effects of superimposing a deficiency of vitamins B complex and E on the neurosyphilis. Similarities are pointed out between tabes and the alcoholic myeloencephalopathies,

which have been thought to be due to deficiency in the vitamin B complex. Stone believes that the vitamin B complex and vitamin E may have a synergistic action and that vitamin E may have a function in maintaining or restoring normal myelination. CHODOFF, Washington, D. C. [ARCH. NEUROL. & PSYCHIAT.].

THE THERAPY OF LYMPHOGRANULOMA VENEREUM. R. BRANDT, South. M. J. **34**:941 (Sept.) 1941.

The author states that the acute bubo of lymphogranuloma venereum is profoundly influenced by chemotherapy with sulfanilamide and derivatives and compounds of it. Late manifestations do not occur after intensive early treatment, but chronic lesions, especially rectal strictures, often develop without preceding acute manifestations.

Ulcerative and hyperplastic lesions are less favorably influenced. Those of short duration usually yield to prolonged chemotherapy, possibly reenforced by vaccinotherapy or physical therapy. Chronic ulceration and elephantiasis are, however, resistant to therapy.

In rectal stricture, pain, rectal leukorrhea and general complaints respond, and often completely yield, to chemotherapy. Stenosis is influenced by mechanical dilatation.

Patients seen in the acute stage of lymphogranuloma venereum may expect complete healing. The treatment of neglected lesions or those developing without a preceding acute state is less promising.

SCHLUTZ, Chicago [AM. J. DIS. CHILD.].

AVITAMINOSIS IN RELATION TO DISEASES OF THE SKIN. J. W. MCNEE, Brit. J. Dermat. **54**:159 (June) 1942.

The author states that dermatologists have two problems to face in connection with vitamins: 1. Are any of the known diseases usually seen by dermatologists due to deficiency of one or more vitamins? 2. When a large area of skin is abnormal from a dermatologic disease over a long period can avitaminosis follow as a sequel?

VITAMINS AND DISORDERS OF THE SKIN. GODFREY BAMBER, Brit. J. Dermat. **54**:163 (June) 1942.

There seems to be little justification for administration of vitamins in cases of diseases of the skin except in instances of the classic and forme fruste examples of avitaminosis. The author states that keratosis pilaris, lichen pilaris, lichen spinulosus and ichthyosis follicularis are merely descriptive terms for the cutaneous manifestations of vitamin A deficiency. Vitamin B therapy is indicated in ariboflavinosis and pellagra. A follicular-papular rash may be a sign of scurvy. There are no changes in the skin that have been attributed primarily to the absence of vitamin D.

BLUEFARB, Chicago.

LUPUS VULGARIS. ROBERT AITKEN, Brit. J. Phys. Med. **4**:66 (May-June) 1941.

The incidence of this disease in the dermatologic department of the Royal Infirmary of Edinburgh has varied from 0.5 to 1.0 per cent in the last ten years. Fifteen to twenty years ago the percentage varied from 2.8 to 4.0. In an analysis of 294 cases, it was found that in almost 25 per cent the lupus occurred in the age period of 6 to 10 years, and more than half of it began during the school life of the child. It affected the face in 77 per cent of the cases.

A diet rich in vitamins and the careful use of caustics, of tuberculin and of general ultraviolet irradiation are recommended. Treatment with roentgen rays is condemned.

Local treatment with a Finsen-Lomholt lamp is found most satisfactory. This is a carbon arc lamp with a complex lens septum.

The author presents 2 case studies.

HARTMAN, Cleveland [AM. J. DIS. CHILD.].

DERMATITIS HERPETIFORMIS DUHRING IN A NEWBORN INFANT. H. WILLI and W. BURCKHARDT, Kinderärztl. Praxis **12**:144 (May) 1941.

This is a description with photographs of a newborn infant (weighing 3,380 Gm.) with dermatitis herpetiformis. The diagnosis was established by the characteristic rash as well as by the following findings: (1) The content of the vesicles was sterile; (2) in this fluid and also in the blood an extreme eosinophilia (up to 46 per cent eosinophils) was found; (3) a patch test with 10 per cent potassium iodate in petrolatum led to the production of a herpetiform lesion on the skin. The disease lasted for over six months. The baby gained weight, however, and progressed normally in spite of the extensive cutaneous lesions. Treatment of the skin consisted of potassium permanganate baths and applications of 1 per cent silver nitrate and of powder.

HEYMANN, Cleveland [AM. J. DIS. CHILD.].

HISTAMINE CONTENT OF BLOOD AND URINE IN CUTANEOUS DISEASES. S. MITUMOTO, Jap. J. Dermat. & Urol. **49**:25 (March 20) 1941.

The author examined the histamine content of the urine and blood of patients with different cutaneous diseases. The histamine content was increased proportionately to the intensity and extension of the dermatitis. In very old persons and children there was a slight increase in the histamine content; otherwise age and sex did not have any influence on the histamine in blood and urine. The amount of excreted histamine in the urine was somewhat higher than that in the blood. In cases of urticaria the histamine content was relatively high. It was higher in edematous dermographism than in the nonedematous form. In some cases of eczema and dermatitis medicamentosa the increase of the histamine content in the blood was high when compared with the degree of cutaneous involvement.

BLOOM, New York.

Society Transactions

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Feb. 26, 1942

Pemphigus Vulgaris. Presented by Dr. Benjamin Levine.

A. H. L., a Jew aged 55, was first seen on July 29, 1941, at which time he had superficial ulcerations on his nose with superimposed crusts and extensive ulcerations of the buccal mucosa of several weeks' duration. One week after his first visit vesicular and bullous lesions developed on the scalp and cheeks. The temperature, pulse and respirations were normal. One week later larger vesicles and blebs appeared on his body. They contained clear fluid and were located on a noninflammatory base. There was little or no itching. The lesions became more extensive, and the patient was admitted to Mount Sinai Hospital on August 26.

While he was in the hospital the lesions became more numerous, particularly on the hands, feet and neck. Some lesions also developed in the upper respiratory passages. The patient was given sulfanilamide, and on September 8 the level of the drug in the blood reached 9.9 mg. per hundred cubic centimeters. On September 14 the administration of sulfanilamide was discontinued because of toxic symptoms. The patient was given repeated saline infusions together with 5 per cent dextrose intravenously. In the meantime numerous vesicles and blebs developed on the back, abdomen and thighs. He was then given injections of riboflavin, the dose starting at 1 mg. twice a day and being later increased to 3 mg. Beginning on September 21 he was given highly concentrated viosterol, receiving a total of 500,000 U. S. P. units of vitamin D daily. Vitamin B complex was administered by mouth, and 1 cc. of liver extract was administered parenterally daily. His condition became progressively worse, and then 100 cc. of whole blood was given by transfusion daily. Under this regimen he showed decided improvement. The administration of vitamin D was discontinued for a short time, and he again became worse. He received three more blood transfusions, a total of 1,400 cc. The lesions, which had been profuse, on the arms and legs, feet and hands, as well as those on the nose and neck, cleared. Within a week he had an exacerbation, with lesions developing on his hands, feet and back. Those on the back became so extensive that there was little normal skin left in that region. The feet became extensively involved and edematous. He became extremely emaciated and was finally unable to take any food. He was given 250 cc. of blood plasma and 1,000 cc. of 5 per cent dextrose solution by way of the bone marrow. During the past few weeks some of the lesions have assumed the aspect of pemphigus foliaceus. He received in addition to the aforementioned medications intravenous injections of iron cacodylate and intramuscular injections of a preparation of thromboplastin.

Histologic examination showed the superficial layers of the epidermis separated from the deeper layers forming a round vesicle. The deeper layers of the corium showed several small similar defects. All the cells of the midportion of the corium showed a moderate degree of edema. The rete pegs were short. There was a round cell infiltration about the hair follicles and small vessels.

The hemogram revealed a moderate degree of secondary anemia, and the white blood cells varied from 12,750 to 23,350. Differential blood counts were

not remarkable with the exception of the eosinophils, which gradually rose to 10 per cent. Chemical studies of the blood showed values essentially within normal limits. Blood cultures repeatedly gave negative results.

The patient died on Feb. 7, 1942. The autopsy observations were unusually meager. There were superficial ulcers of the pylorus and of the stomach. The lungs showed healed apical tuberculosis. The heart muscle was flabby from extreme exhaustion. The kidneys showed a moderate degree of degenerative changes, and microscopically there were some deposits of calcium, which could have been caused by toxemia or by large doses of viosterol.

DISCUSSION

DR. H. N. COLE: Dr. Levine asked me to see this patient in consultation. At that time he presented the picture of pemphigus foliaceus. He was very ill, and Dr. Levine had already done practically everything that is ordinarily done for these patients.

DR. H. J. PARKHURST, Toledo, Ohio: I understand that germanin was not tried. I should like to ask what the experience of the members has been in the use of this drug.

DR. R. E. BARNEY: I presented a patient at the meeting at St. Luke's Hospital, in January of last year, who was treated with germanin. I had tried everything else without success, and the patient had a remission promptly and is well today without any lesions. Reports in the literature on the use of germanin vary as to its usefulness.

DR. FRANK J. LACKSEN, Columbus, Ohio: My associates and I tried germanin in at least 7 cases of the bullous type at Bellevue Hospital in New York, without results. However, we had some patients with the foliaceous type who had remissions, and when last seen their condition was still in remission.

DR. H. N. COLE: My associates and I have given this drug to 2 patients with pemphigus vulgaris. Both died of their disease.

Dermatitis Factitia. Presented by DR. DONALD N. MACVICAR.

M. D., a 19 year old white girl, presented from the department of dermatology and syphilology, University Hospitals, complains of an ulcer of the left forearm. Two years previously, following a "brush burn," the ulcer appeared and has persisted until the present time. Numerous types of local therapy were applied, including zinc peroxide, sulfathiazole powder, cauterization and a skin graft. At no time did the ulcer heal entirely. Just previous to her admission to the hospital amputation of the arm had been advised by her physician.

Examination reveals a well developed and well nourished white girl. On the midportion of the left forearm, immediately overlying the ulna, is a sharply defined round ulceration, 5 cm. in diameter. The base is red and granulating and covered with a small amount of purulent material. In the center of the lesion a small depressed area is seen. Around the ulcer are three round scars varying from 1.5 to 3 cm. in diameter.

Except for a slight elevation of the total leukocyte count, the hemogram was normal. The reaction to a Kline exclusion test of the blood was negative. Aerobic and anaerobic cultures of material from the ulcer grew only Staphylococcus aureus. Roentgenograms of the left arm revealed a rarefaction of the ulna beneath the ulcer.

DISCUSSION

DR. H. A. HAYNES JR., Akron, Ohio: I can give some additional history, which may throw some light on this case. I first saw the patient two years ago, approximately one month after she had received a subcutaneous injection in the forearm of either morphine or caffeine. It was apparently given after a hysterical attack. At this time there was an ulcer about the size of a silver dollar on her forearm going down to and directly between the muscles. The borders were

undermined and anaerobic organisms were found on culture. It did not respond to the administration of sulfonamide drugs. After two or three weeks it continued to extend. A surgeon excised the entire ulcer and infected area widely and cleanly, and the infection appeared to go up as far as the elbow. After this zinc peroxide paste dressings were used, and she got along well. The area of excision granulated with no evidence of infection. Skin grafts were performed, and the area healed completely. After about six months a new slough and ulcer developed in the same area. Again excision was performed and zinc peroxide paste dressing applied, and again the lesion healed. I have not seen her for about a year. I am not certain that she has dermatitis factitia.

DR. J. R. DRIVER: This girl was placed in the hospital on the theory that this lesion was self inflicted. Occlusive dressings were used, and in approximately two weeks the lesion healed about 50 per cent. The girl is subject to attacks of hysteria. She is emotionally and nervously unstable. The family physician had been looking after her for some time, had had no success and suggested amputation of the arm. She was more than satisfied to have it performed.

DR. H. A. HAYNES JR., Akron, Ohio: I am inclined to agree with the diagnosis as presented, but at the beginning there appeared to be a subcutaneous infection following the hypodermic injection given during a hysterical attack.

A Case for Diagnosis (Toxic Erythema? Drug Eruption?). Presented by DR. HUGO HECHT (by invitation) and DR. E. GLICKSBERG (by invitation).

G. S., a white woman aged 38, has had a generalized eruption of four days' duration. She states that she first noticed a red itching eruption on the chest. The lesions rapidly spread to involve the face, trunk and extremities. There are no palmar or plantar lesions. Twelve hours after the onset the patient took 2 ex-lax tablets and a tablespoonful of magnesia magma.

The cutaneous examination reveals a maculopapular erythematous eruption involving the face, trunk and extremities. Secondary excoriations are present.

DISCUSSION

DR. JOHN E. RAUSCHKOLB: This patient has an eruption limited chiefly to the covered parts of the body. I offer in differential diagnosis lichen planus, pityriasis rosea or a papular type of urticaria. The lesions are a little bit too papular for pityriasis rosea, though there was a sudden onset in the area of the chest. The patient stated that the eruption started immediately after the application of a sachet powder in the region of the breasts. It may be that there is a sensitivity to the powder that she applied. Patch tests with the powder are indicated.

DR. H. J. PARKHURST, Toledo, Ohio: I do not believe that this patient has pityriasis rosea or contact dermatitis. Clinically the eruption looks like a toxic erythema. A drug eruption can be eliminated inasmuch as the patient gave no history of taking medication preceding the onset.

DR. BENJAMIN LEVINE: The patient stated that she used the sachet powder on her chest. If this eruption were a contact dermatitis one would expect it to be more intense in this area. However, the lesions are more profuse over the lower part of the abdomen. According to the history, she had some pruritus and then took a laxative containing phenolphthalein, and immediately afterward the eruption became extensive. Apparently this eruption is a toxic erythema, but I do not think that phenolphthalein is responsible for it. I favor a diagnosis of erythema multiforme.

DR. GEORGE CURTIS: I favor a diagnosis of toxic erythema. She shows a pronounced dermographia.

DR. HUGO HECHT (by invitation): Monday evening she took some ex-lax, and the next day this eruption covered the entire body. The eruption resembles

somewhat pityriasis rosea, but it would take some time to develop from a primary lesion, usually ten days to two weeks. I think it is toxic erythema caused by phenolphthalein.

A Case for Diagnosis (Angiokeratoma?). Presented by DR. BENJAMIN LEVINE and DR. HUGO HECHT (by invitation).

S. H., a man aged 55, was first seen on Feb. 7, 1939, at which time he had numerous enlarged follicular openings in the roof of the mouth and also several pea-sized umbilicated lesions that were painful. He has had severe diabetes mellitus since August 1937.

At present there are on the hard palate a score or more pinhead-sized or larger hyperkeratotic whitish papules, and in the center of each lesion there is a small bright red area.

Histologic examination showed the surface epithelium to be thickened. The outermost cells showed abundant blue-stained granular material. External to this there was a prominent layer of necrotic epithelium. In about the center of the section there was an area about 0.5 mm. in diameter which showed numerous dilated thin-walled blood vessels. Regional to it in places there was a small artery with degenerative and necrotic changes in a portion of the wall. Adjacent to this telangiectatic area the surface epithelium was not only thickened but also considerably infiltrated by wandering cells. There was also a mucous gland well below the surface epithelium whose duct was considerably dilated.

The Kline reaction of the blood was negative. The urinalysis revealed a large amount of sugar. The hemogram was normal.

The original pea-sized lesions were removed by the actual cautery, but lesions recurred not only at the original sites but in increasing numbers nearby. They were also treated with 10 per cent silver nitrate solution and sprayed with a mixture of gentian violet (3 per cent), brilliant green (1 per cent) and acriflavine base daily for one month. The pain diminished and the lesions regressed slightly. Ultraviolet radiation from a quartz mercury vapor glow lamp (cold quartz lamp) was applied to the lesions for six months, with but slight benefit. On April 8, 1941 roentgenotherapy was instituted. The patient received 150 r at intervals of two to three weeks, a total of 3,300 r.

DISCUSSION

DR. E. W. NETHERTON: The lesions are similar to those that occur on the palate in keratosis follicularis. However, the histologic section did not verify that opinion.

DR. H. J. PARKHURST, Toledo, Ohio: Clinically, many of the lesions on the palate looked like tiny vesicles to me, and the histologic examination showed that there were many dilated vessels in the section. I favor a diagnosis of lymphangioma.

DR. HUGO HECHT (by invitation): Lymphangioma is very rare on the hard palate. Darier mentioned it. Of course, it is ordinarily seen on the tongue when located in the mouth. The commonest location of angiokeratoma is on the scrotum. Lesions are found sometimes on the hands and feet. Histologically, the lesion resembles angiokeratoma.

DR. H. N. COLE: I have encountered several cases of leukoplakia on the hard palate which assumed this papular appearance. This man is a heavy pipe smoker. I should treat the lesions with the electrocautery and suggest that he stop smoking. I believe the histologic appearance is consistent with this diagnosis. The slide I examined was not satisfactory.

Lupus Vulgaris. Presented by DR. E. W. NETHERTON and DR. GEORGE H. CURTIS.

E. B., a man aged 74, was first seen on Jan. 27, 1942. His chief complaint was a symptomless eruption involving most of the left side of the face, the back of the neck, the under surface of the chin and the posterior surface of the right leg. He had never married. His family history was unimportant, and the past

history was irrelevant except for gonorrhea thirty years ago and a question of a penile lesion which he had in his early youth. He has never received antisyphilitic treatment or had symptoms or manifestations which were interpreted by his physician as probably being syphilitic.

His present illness began five years ago as a red papule beneath the left eye. The initial lesion enlarged by peripheral extension until it involved most of the left side of the face. The lesion has become a large erythematous scaly area without any tendency toward ulceration. In the past year subcutaneous and cutaneous nodules have developed on the left anterior portion of the neck just beneath the chin and also on the posterior surface of the neck back of the right ear. A short time later a similar lesion developed on the posterior surface of the right leg, including the thigh.

There is a large, light red, well demarcated, infiltrated, slightly scaly granulomatous plaque extending from the left temple and just in front of the ear to involve the whole side of the face and extending on to the neck just below the margin of the lower jaw. There is a slight ectropion of the lower left eyelid. The margin beneath the left nostril is sharply defined and slightly rolled. Beneath the left side of the chin on the anterior portion of the neck are groups of small adherent crusts surrounded by a dull red erythema which is not sharply demarcated. This erythematous crusted lesion is situated on the central portion of a deeply seated cutaneous and subcutaneous nodule which is poorly demarcated. A similar lesion is present on the posterior surface of the neck just back of the right ear, and one on the posterior surface of the right thigh. There is a mild rhinophyma with dilatation of the follicles on the nose and numerous comedos. Apple jelly nodules cannot be seen on diascopic examination.

The urine and the hemogram were normal. The Wassermann and Kahn reactions of the blood were negative. A roentgenogram of the chest was normal.

Histologic examination of tissue taken from the border of a large plaque in the region of the left temple showed moderate acanthosis. However, in most of the section there was atrophy of the epidermis with almost complete obliteration of the interpapillary pegs. There was a thin layer of parakeratosis in a few areas. Some of the pilosebaceous follicles were dilated and contained hyperkeratotic plugs. The basal cell layer was intact. There was a diffuse chronic inflammatory reaction involving the whole corium. The cellular infiltration consisted of poorly circumscribed areas of epithelioid cells and lymphocytes. There were no tubercles surrounded by a zone of lymphocytic infiltration; however, there were small collections of epithelioid cells and giant cells in the deeper portion of the corium. These areas were interpreted as being small tubercles. There were numerous giant cells of Langhans' type scattered throughout the corium. There were no areas of necrosis. There was a zone of lymphocytic infiltration surrounding the pilosebaceous follicles. The most striking change in the corium was the presence of large areas of hyalinization or basophilic degeneration of the fibrous tissue in the upper portion. Acid-fast bacilli were believed to be seen in specially stained sections.

Urticaria Pigmentosa. Presented by DR. IRVING SCHONBERG.

B. T., a white man aged 26, has had an eruption on his body for the past nine years. He noticed the eruption first on the right breast and then on the thighs. During the past two years the lesions have spread over the entire body. On the forehead and face there has been a rapid progression in pigmentation and itching.

On the trunk, extremities and forehead are numerous discrete copper-colored macules about the size of a split pea or a little larger. On being stroked the lesions become urticarial and pruritic.

The basal metabolic rate was —9 per cent. The blood sugar content was 79 mg. per hundred cubic centimeters. The hemogram was normal. The urine was normal. Roentgenotherapy produced moderate improvement.

DISCUSSION

DR. J. E. FISHER: I saw this patient about four years ago, and there is not much change in the condition today.

DR. BENJAMIN LEVINE: I have a patient with urticaria pigmentosa which has lasted more than twenty years. Roentgenotherapy has been of definite value; the disease is less extensive than formerly, and exacerbations are fewer.

DR. IRVING SCHONBERG: I have observed this patient for the past year, and during this time it seems that the pigmented areas are becoming more profuse on the forehead. He has been under various types of treatment. I have noticed that the eruption is aggravated in the summer when he gets tanned. Considerable roentgenotherapy has been given with little if any beneficial effect.

C. G. LAROCCO, M.D., *President*

J. E. RAUSCHKOLB, M.D., *Secretary*

JAMES R. DRIVER, M.D., *Reporter*

March 26, 1942

A Case for Diagnosis (Discoid Lupus Erythematosus?). Presented by DR. GEORGE M. STROUD III.

L. W., a Negro boy aged 11 years, is presented from the outpatient department of dermatology and syphilology, University Hospitals, with a facial eruption of one month's duration. There are no subjective symptoms.

There are symmetric depigmented scaly slightly indurated patches on the nose and cheeks. A general physical examination revealed no abnormalities.

Histologic examination showed parakeratosis with some dilatation and plugging of the follicles. There were irregular acanthosis and microscopic vesicles in the upper portion of the epidermis. Edema of the epidermal cells was present, and in places there was migration of inflammatory cells into the epidermis, with loss of definition of the corioepidermal junction. Focal areas of small round cell infiltration were present in the upper part of the corium, especially in the region of the follicles.

Topical applications of a coal tar, ammoniated mercury ointment and of a sulfur cream have produced no significant change.

DISCUSSION

DR. H. A. HAYNES JR., Akron, Ohio: I believe a specimen for biopsy taken from the papular lesions on the forehead may give additional evidence of value in diagnosis.

DR. J. R. DRIVER: Clinically the eruption resembles lupus erythematosus. However, one would not expect to see these changes in lupus erythematosus of only one month's duration. I should treat the disease as seborrheic dermatitis, employing roentgenotherapy. Further specimens for biopsy should not be taken because of the tendency toward keloid formation in Negroes.

DR. C. L. CUMMER: I agree with Dr. Driver. I thought the histologic picture was suggestive of seborrheic dermatitis.

Syringocystadenoma. Presented by DR. GEORGE M. STROUD III.

C. G., a Negress aged 40, presented from the department of dermatology and syphilology, University Hospitals, states that she has had asymptomatic lesions on the trunk since childhood. A sister has similar lesions.

On the chest and upper part of the abdomen are many raised, rounded papules measuring from 4 to 10 mm. in diameter. The surface of these lesions is shiny, and there is a fine crinkling of the overlying epidermis.

Histologic examination showed slight atrophy of the epidermis and many cystic areas in the reticular corium, lined with deeply staining epithelial cells and containing fluid. Scattered among them were nests of epithelial cells, some of which seemed attached to the cysts. Only a few of the nests had the so-called "tadpole tail" appearance.

DISCUSSION

DR. R. E. BARNEY: The case is interesting because of the clinical resemblance to lichen planus. The histologic picture is characteristic of the disease as presented.

Progressive Pigmentary Dermatosis. Presented by DR. GEORGE M. STROUD III.

D. B., a Greek housewife aged 44, presented from the department of dermatology and syphilology, University Hospitals, complains of a pruritic pigmentation of the legs of one year's duration. For the past year she has noticed paresthesias in the toes and fingers. She states that the eruption began on the feet and spread proximally.

On the dorsa of the feet, ankles and lower portions of the legs is a diffuse brown pigmentation with tiny interspersed telangiectases. There are some lichenification and scaling over the ankles.

Histologic examination of a section of involved skin revealed perivascular and focal infiltration of lymphocytes in the corium.

DISCUSSION

DR. H. G. MISKJIAN: On close examination one finds that there is hyperpigmentation with little red dots around the lesions. There is absence of dermatitis, edema of the skin or inflammatory reaction of any kind. This is the picture described by certain French authors as capillaritis. Small hemorrhages in the skin result in hyperpigmentation. Capillaritis is a general term. The condition is seen also in other cutaneous diseases. This condition falls into the group classified as Schamberg's progressive pigmentary disease.

DR. OTTO SCHMIDT: I have recently read an article (Touraine, A.: Les capillarites en dermatologie, *Bull. Soc. franç. de dermat. et syph.* **44**:837-965, 1937) in which the concept of capillaritis was carefully developed. Included in this category were many diseases that are ordinarily considered separately in their causation and course of development. The concept of capillaritis helps one to a better understading of many diseases presenting vascular changes and has been popularized in France during the past fifteen years.

DR. E. W. NETHERTON: What does Dr. Schmidt consider the cause of this disease?

DR. OTTO SCHMIDT: The causes may be as varied as the diseases mentioned. Any chronic or acute disease may cause capillaritis or almost any known and unknown agent can cause diseases of the capillaries, as evidenced by biopsy and clinical appearance.

Scleroderma, Generalized Progressive Type. Presented by DR. DONALD N. MACVICAR.

M. T., a Negress aged 33, was first seen in the department of dermatology and syphilology, University Hospitals, in 1936, at which time a diagnosis of late latent syphilis was made. Antisyphilitic therapy was administered, and in 1938 she was put on probation, to return for periodic reexaminations. In November 1940 she entered the hospital complaining of hardening of the skin and aching pains in the fingers and arms. A diagnosis of scleroderma was made, and since that time there has been slow progression of that process.

The entire skin of both arms and to a lesser extent that of the face and neck is smooth, shiny and hard. The skin is fixed to the subcutaneous tissues, and there is limitation of motion at the elbows. Spotty areas of depigmentation are present.

The hemogram and urine were normal. The Kline and Wassermann reactions of the blood were strongly positive. The blood creatinine amounted to 1.6 mg. and the urinary creatinine to 48.7 mg. per hundred cubic centimeters. Roentgenograms of the hands and arms revealed no abnormalities. The basal metabolic rate on two occasions was +6 per cent and +23 per cent. Tissue removed from the muscle of the right arm for histologic study was normal. Histologic examination of a section of the involved skin revealed changes characteristic of scleroderma.

Alpha tocopherol acetate with pyridoxine was given orally, with no appreciable effect. Roentgenotherapy, a total dose of 1,050 r in divided doses, over the lumbar and the upper part of the dorsal region produced no effect. The disease has progressed steadily.

DISCUSSION

DR. E. W. NETHERTON: Has the patient ever shown any signs of dermatomyositis?

DR. DONALD N. MACVICAR: The patient was hospitalized for about one month, and two specimens for biopsy from deep portions of the muscle showed no lesions of dermatomyositis.

A Case for Diagnosis (Lymphoblastoma?). Presented by DR. DONALD N. MACVICAR.

S. M., a Negro aged 52, complains of swelling of the right leg. He states that eight months ago he noticed a hard tender mass in the right groin, followed by progressive swelling of the right leg. This mass has persisted, and several similar but smaller masses have appeared and disappeared in the axillas and on the shoulders and upper part of the back. For the past year he has had intermittent generalized pruritus.

Vitiligo is almost generalized, and only a few scattered areas of pigmentation are present. On the skin of the abdomen near the left costal margin is a flat black nevus, 1 by 3 cm. In the right inguinal region many hard, enlarged, matted nodes are felt. Several smaller nodes are palpable in the left inguinal area. The right leg is swollen to approximately twice the size of the left. Just below the right inguinal ligament is a hard irregular subcutaneous mass, the size of a hand. The skin overlying this mass is in places red and scaling. There are two purulent draining ulcerations, the site of wounds made for removal of tissue for biopsy. Similar but smaller masses are present on the right calf and in the left axillary and right supraclavicular areas.

The urine was normal. The hemogram revealed 25 per cent large monocytes in the differential count. The Kline reaction of the blood and the reaction to a Frei intradermal test were negative. Roentgenograms of the chest, pelvis, spine and skull revealed no abnormality except moderate enlargement of the heart. Histologic examination of a lymph node removed from the right inguinal region showed hyperplasia of the endothelial cells and multiple areas of necrosis surrounded by zones of granulation tissue. A few giant cells with purple-staining cytoplasm and three to four nuclei were present. Histologic examination of material from the mass below the right groin revealed some hyperkeratosis and parakeratosis with moderate acanthosis. In the corium and subcutaneous tissue were many extensive areas of infiltration with lymphocytes. Areas of widespread necrosis were also present.

DISCUSSION

DR. C. L. CUMMER: Did the term monocyte include all types of large mononuclear cells?

DR. DONALD N. MACVICAR: There is a definite increase in the monocytes. This was not interpreted as evidence of a leukemia.

DR. JOHN RAUSCHKOLB: The ulcerative condition now present in the right groin is suggestive of chronic chancroidal infection.

DR. DONALD N. MACVICAR: The ulceration is secondary to the removal of an inguinal lymph node.

DR. HENRY A. BRUNSTING, Toledo, Ohio: My impression is that this patient has lymphoblastoma, perhaps Hodgkin's disease or lymphosarcoma. The ultimate diagnosis will depend on further laboratory studies.

DR. J. R. DRIVER: The disease started in the right inguinal region and clinically is a granuloma. Further histologic studies of the tumor mass in the groin are indicated.

DR. C. L. CUMMER: A monocyte count of 25 per cent, I believe, has definite significance when associated with adenopathy such as that seen in this case.

DR. E. W. NETHERTON: I agree with Dr. Cummer. I should call this patient's disease monocytic leukemia. I had a patient about six months ago with ulcerated lesions similar to this patient's and with a similar blood count. The hematologists at the Cleveland Clinic also agreed to a diagnosis of monocytic leukemia. Another biopsy may show some of the cells seen in monocytic leukemia.

Lymphosarcoma with a Prurigo-Like Cutaneous Eruption. Presented by DR. DONALD N. MACVICAR.

E. C., a Negro aged 57, presented from the department of dermatology and syphilology, University Hospitals, was first seen in August 1940, complaining of pruritus and swellings in the neck and groin. A diagnosis of lymphosarcoma was made and substantiated by histologic examination of a lymph node. He states that for the past three years he has had severe pruritus and that small "lumps" have appeared and disappeared on his arms and legs. In the past six months larger transient nodules have periodically appeared on the chest and on the upper half of the abdomen.

There is generalized enlargement of the superficial lymph nodes. Scattered over the arms, legs and neck are many round indurated hyperpigmented papules, 3 to 4 mm. in diameter, with excoriated tops. On the chest and upper part of the abdomen are eight to ten larger hard deep nodules.

The urine was normal. The hemoglobin content of the blood was 73 per cent, and the erythrocytes numbered 3,700,000 per cubic millimeter. The leukocyte count was 4,250, with 16 per cent eosinophils. The Kline reaction of the blood was negative. Repeated biopsies of the cutaneous lesions revealed focal areas of infiltration in the corium and subcutaneous tissue composed of eosinophils, polymorphonuclear leukocytes, lymphocytes, plasma cells and large mononuclear cells.

DISCUSSION

DR. J. R. DRIVER: The diagnosis of lymphosarcoma was made while the patient was in the medical ward of the hospital. If this diagnosis were correct one would expect to find involvement of the tonsils, particularly since the cervical lymph nodes are enlarged. However, one finds no such involvement. On the other hand, the prurigo-like exanthem the patient exhibits is clinically characteristic of Hodgkin's disease. When one considers this combined with the other manifestations, a diagnosis of Hodgkin's disease is indicated.

DR. R. E. BARNEY: My impression of the case is similar to that of Dr. Driver. I believe that the patient may well have Hodgkin's disease, and my conception of the cutaneous eruption was that it was an id.

Granuloma Inguinale; Latent Syphilis. Presented by DR. DONALD N. MACVICAR.

F. S., a Negro aged 23, presented from the department of dermatology and syphilology, University Hospitals, was first seen in June 1940, at which time a diagnosis of early mucocutaneous syphilis was made. From June 1940 to October 1941 he received antisyphilitic therapy regularly to the amount of approximately thirty injections of mapharsen and thirty injections of a bismuth compound. Since October 1941 therapy has been irregular. He has just entered the hospital complaining of penile lesions of three weeks' duration.

On the inner surface of the prepuce is a flat, raised, beefy red lesion, 4 cm. in diameter, with an irregular surface covered by a glairy sanguineous exudate. Regional adenopathy was not remarkable.

The hemogram and the urine were normal. The Kline diagnostic and exclusion reactions of the blood were negative. Smears of the exudate and smears of tissue removed from the lesion revealed Donovan bodies. Repeated dark field examinations of the lesion failed to reveal Spirochaeta pallida.

Histologic examination of tissue removed from the lesion showed diffuse infiltration of the corium with lymphocytes and plasma cells and focal accumulations of polymorphonuclear neutrophils. Large mononuclear cells containing Donovan bodies were seen.

The patient was given five intravenous injections of antimony and potassium tartrate at two day intervals. The lesion became paler and decreased in size along one border.

DISCUSSION

DR. EMERSON GILLESPIE, Canton, Ohio: This case is interesting because as a rule one sees this disease at a much later stage, when considerable destruction has occurred.

DR. JOHN RAUSCHKOLB: In early lesions of granuloma inguinale healing after the administration of antimony and potassium tartrate is usually rapid.

DR. J. R. DRIVER: Healing following therapy with antimony preparations results in a scar which is likely to be the site of recurrences. This is particularly true if therapy is not continued over a long period after the patient is apparently cured. Therefore, I believe, it is advisable to excise these scars whenever practicable. Apparently some Donovan bodies are locked in the scar tissue and sooner or later become active. The suspicious area in the case presented could be removed by circumcision after healing has occurred.

DR. C. G. LAROCCO: Would a circumcision be indicated before healing of the lesion has occurred?

DR. J. E. RAUSCHKOLB: I do not agree concerning circumcision in this case, for the lesion is an early one and there will be little scar formation. In a case of long-standing chronic granuloma inguinale the amount of scarring produced is usually extensive. Excision is not always possible but is indicated in order to eliminate a focus of infection. Long-continued treatment is the best prophylaxis against relapse.

LOS ANGELES DERMATOLOGICAL SOCIETY

KENDAL FROST, M.D., *President*

ARTHUR FLETCHER HALL, M.D., *Secretary*

Dec. 9, 1941

Pustular Folliculitis of the Scalp. Presented by DR. M. J. WOLFF.

A. H., a 19 year old white youth, has suffered from his present eruption for about one year in spite of treatment. He shows scattered pinhead-sized pustules about the hair follicles of the scalp. Itching usually is mild but at times is severe. The urine and the blood count were normal. Treatment has consisted of local medications, including gentian violet solution and sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) ointment. The patient is sensitive to mercury.

DISCUSSION

DR. SAUL ROBINSON: Has sulfathiazole been given by mouth? Or staphylococcus toxoid? I suggest giving this treatment in this case. I think that an

eruption like this is probably an allergic response to staphylococci. I think that use of sulfathiazole internally is the only way it can be cleared up.

DR. M. E. OBERMAYER: At the risk of being misunderstood, I think that this disease is not a purely local condition; if it were, local treatment would have cleared it up in a short time. I think there is a functional element in this case. The patient is nervous; he studies hard and never goes to bed before midnight. When he went on a vacation to Lake Tahoe the eruption cleared up completely without treatment. I think that is some indication that the disease is not infectious. I think he should be given daily generalized ultraviolet radiation and sedatives and his resistance against staphylococci built up with injections.

DR. BEN A. NEWMAN: The diagnosis seems to be a simple problem, but it is really difficult. Each patient with this disease seems to present a rather typical picture: follicular lesions in groups, always appearing in the same manner on the scalp and uniform in the stage of development. Itching is not usual in a folliculitis or pustular type of eruption. The lesions will persist for several weeks and then disappear, and later a new crop will develop. Almost any form of treatment has the same effect or no effect. I have 2 patients now with the same condition. There are no foci of infection. One patient left the city entirely well and then sent me a letter asking for suggestions as to treatment; the condition is apparently worse than ever. It is not in an infectious group of eruptions; still it is hard to believe that it is a functional disease.

DR. SAUL ROBINSON: I recently saw a child of 2½ years with the same morphologic picture in the scalp of one and one-half years' duration. The only thing which cleared the lesions was a change in the diet. I eliminated various foods and made a change in the milk. The picture in the case presented is definitely that of a staphylococcic folliculitis. I wonder if food allergy could play a part.

DR. KENDAL FROST: I was wondering if the patient does not have acne necrotica miliaris; that is a functional disease.

DR. BEN A. NEWMAN: There is no scarring or atrophy.

DR. M. E. OBERMAYER: Do you not think the eruption is a sycosis?

DR. BEN A. NEWMAN: The eruption never becomes confluent; the lesions do not become crusted over as sycosis will do. It is not eczematous; it always appears as pustules and clears up and leaves apparently normal skin. It is rather a strange picture and it should deserve more attention.

DR. M. J. WOLFF: This patient had been under the care of another dermatologist for six months, and I have treated him for six months. I have used a combination of salicylic acid and sulfur, sulfathiazole ointment and gentian violet. The condition cleared up with gentian violet. When I stopped giving it the lesions appeared the same as before. I gave him roentgen therapy without apparent benefit. I noted particularly what Dr. Obermayer said about the disease's being functional. I might say that the patient is cooperative. I do not feel that the condition is a functional disease, and I do not think it is a sycosis. It looks like an infection that would clear up readily. The patient is in good health.

Trichophyton Purpureum Infection of the Nails. Presented by DR. NELSON PAUL ANDERSON and DR. SAMUEL AYRES JR.

B. H., a 20 year old white youth, first noted involvement of the toes about the nails five years ago. A short time later there occurred undermining of the nails; later the patient injured his right thumb nail, which has never returned to a normal state. Soon the right index finger nail was involved, and about three months ago the right middle finger nail was attacked. Previous therapy received elsewhere consisted of local applications and unfiltered roentgen therapy. Examination now reveals an eroding process involving the nails of the thumb, index finger and middle finger of the right hand and the ring finger of the left hand.

The left great toe nail is also involved, as well as the left little toe nail. All of the toe nails of the right foot are involved except that of the second toe. Scrapings from the finger nails have been negative for fungi on two occasions. Scrapings from the toe nails have been positive on two occasions. Culture on Sabouraud's medium of material from the toe nails revealed Trichophyton purpureum.

DISCUSSION

DR. NELSON PAUL ANDERSON: This boy is being kept out of the air corps because of his finger nails. He is presented for suggestions as to how to cure him.

DR. HERBERT LAWRENCE (by invitation): What is being done?

DR. KENDAL FROST: Local applications and unfiltered roentgen therapy are being given.

DR. BEN A. NEWMAN: You have had quite a bit of experience with avulsion.

DR. KENDAL FROST: Not with the idea that it will clear the ringworm, but I do think that will make it easier to treat; in that way one can get right into the nail. In the case of 1 young man, I avulsed all of his finger nails. About one third of them grew back infected. I used chrysarobin and iodine and other strong fungicides until they were grown. I have seen some finger nails with ordinary dermatophytoses but none like these; they are extremely resistant to treatment.

DR. NELSON PAUL ANDERSON: I do not know of any one's curing this condition on the skin, let alone in the nails.

DR. ANKER K. JENSEN: How contagious is the disease?

DR. KENDAL FROST: I do not know.

DR. HERBERT LAWRENCE (by invitation): At the Los Angeles County Hospital recently I have observed a few cases of onychomycosis. I used 5 per cent chrysarobin with daily scraping by the patient with a piece of broken glass so that the nail is kept paper thin. In two or three weeks I have had a couple of patients respond. I am not in a position to say whether the infecting organism was T. purpureum.

DR. M. E. OBERMAYER: I am interested in the piece of broken glass. In Chicago I used an electric motor; with this the filing down is done in a minute or two and is much better than with glass. I am not in favor of avulsion. Filing has hastened the clearing up of fungi in nails. The nail is a dead structure and filing it down as thin as possible eliminates a large number of organisms. Then local application will kill the ones on the surface.

KENDAL FROST, M.D., *President*

ARTHUR FLETCHER HALL, M.D., *Secretary*

Jan. 13, 1942

Granuloma Annulare. Presented by DR. SAUL ROBINSON.

I. B., a 33 year old white woman, first noticed pale pink irregularly annular lesions on her buttocks ten years ago. Similar lesions, such as she shows tonight, have come and gone intermittently on the buttocks, thighs and wrists. The present attack has involved the wrists for two years and the buttocks and thighs for eight to ten months. There have been no subjective symptoms.

There has been no response to treatment with solution of potassium arsenite U. S. P. and roentgen rays. Histologic examination ten years ago revealed a picture compatible with granuloma annulare.

Granuloma Annulare. Presented by DR. WALTER F. SCHWARTZ.

F. R. C., a white man, first noticed about fifteen months ago a small circular raised lesion on the back of the right hand. This gradually progressed in size in a circular fashion. Shortly after the onset a few discrete papules appeared on the side and dorsum of the index finger of the same hand. As the large lesion progressed it appeared to clear in the center. There have been no subjective symptoms.

On the dorsum of the right hand is a 3 cm. ringed lesion, violaceous throughout. The margin is made up of numerous firm rounded shining papules, whereas the central cleared portion is almost devoid of papules. Although there is only suggestive atrophy of the skin in the central portion, the skin wrinkles easily. On the lateral and dorsal sides of the index finger of the same hand are several larger papules, a few of which are recently showing central dimpling.

A specimen for biopsy was taken from the active margin of the large annular lesion on the back of the hand one month ago, with 2 per cent procaine hydrochloride with 1:60,000 epinephrine hydrochloride for local anesthesia. Sections of the skin disclosed perivascular round cell infiltration in the cutis. These cells appeared to be, for the most part, lymphocytes. Some were rather large and indicated a monocytic type. There was some degenerative change in the connective tissue, along with some loss of cellularity and possibly necrotic change.

There has been no treatment so far. Since the specimen was taken for biopsy the actively infiltrated margin has almost completely cleared for about ½ inch (1.3 cm.) to either side of the site of incision.

DISCUSSION OF TWO CASES OF GRANULOMA ANNULARE

DR. SAUL ROBINSON: I should like to get some ideas as to therapy. Investigations have been made for foci of infection. The patient has received roentgen and arsenical therapy. The eruption seems to be as profuse as it was two years ago.

DR. ARTHUR FLETCHER HALL: I suggest high vitamin D therapy.

DR. ANKER JENSEN: I had a patient who was given tuberculin and whose lesions began to fade. I continued the tuberculin therapy, and the last time I saw her she was almost well. This is the most extensive case I have ever encountered.

DR. M. E. OBERMAYER: The improvement of the eruption in Dr. Schwartz's case, which apparently resulted from the excision of a specimen for biopsy, is an interesting feature. This observation is in line with that of Massino (*Bol. Soc. de dermat. y sif. Asoc. med. argent.* **4**:31, 1940), who reported a case of granuloma annulare in a 10 year old girl in whom all lesions on her left hand disappeared four days after excision of a specimen for biopsy from that hand. Such rapid spontaneous involution does not seem compatible with the clinical and histologic features of granuloma annulare.

DR. HARRY P. JACOBSON: The spontaneous involution of the lesion following removal of a specimen for biopsy suggests an excellent lead for therapy. The principle involved is one of autovaccination, which in this case was brought into play by the surgical trauma incident to excision of tissue for biopsy. Another therapeutic application of this autovaccination principle could be brought about by the application of solid carbon dioxide to the new lesion in the hope that the resulting inflammatory reaction would bring about involution of the entire lesion.

DR. SAMUEL AYRES JR.: Solid carbon dioxide is often used in treating granuloma annulare, and with fairly good success.

DR. WALTER F. SCHWARTZ: There is some dispute about treating granuloma annulare. I would not have presented this patient if it had not been for the response in the region of the site of removal of the specimen for biopsy. I am glad to hear that there have been experiences similar to this one.

Hyperkeratotic Dermatophytosis. Presented by DR. ANKER K. JENSEN.

E. C., a 48 year old white woman had vesicles on both feet which developed about six months ago. There are now well marginated desquamating lesions on

both feet, especially on the right; these areas are limited mostly to the soles and toes. Vesicles are seen in the margins. She complains of severe pain in the arch of the foot, the skin of which is thickened and indurated.

The Wassermann reaction of the blood was negative. Intradermal oidiomycin and trichophytin tests elicited positive reactions; scales macerated in 20 per cent potassium hydroxide showed mycelium on direct microscopic examination.

DISCUSSION

DR. HARRY P. JACOBSON: The clinical picture presented by this patient is a rather extensive eruption made up of areas of hyperkeratosis associated with some inflammatory reaction, tenderness and pain of the involved parts. Morphologically, and purely from the clinical standpoint, the diagnosis of tinea is unjustified. The statement of the presenter that mycelium was observed under the microscope in fresh wet mount preparations should, of course, not be questioned. However, the mere finding of hyphae in material from the toes or other parts of the feet should not be considered definite evidence of fungous infection. I believe the most likely diagnosis is keratoderma climactericum.

DR. SAUL ROBINSON: I thought pustular psoriasis would have to be ruled out. I suggest that foci of infection be investigated. If the lesion is found to be of bacterial origin, sulfathiazole might be of value.

DR. SAMUEL AYRES JR.: I disagree with what Dr. Jacobson said about the finding of fungi. I have made a habit of making microscopic examination in all cases in which fungous infection is suspected. When fungi are demonstrated I do not ever recall such a case failing to be one of dermatophytosis. One may obtain fungi sometimes on a culture in a case in which the diagnosis is in doubt. When one finds numerous hyphae by direct microscopic examination of scales one must consider a diagnosis of fungous disease. I suggest making a culture in this case, and I should expect to find Trichophyton purpureum.

DR. ANKER JENSEN: I had a good culture, but it dried out. I took it three weeks ago and hoped I could make a diagnosis from it tonight. I found hyphae. The patient must have had ringworm infection at some time.

A Case for Diagnosis (Panniculitis and Sclerodermatous Changes Secondary to Long-Continued Administration of Epinephrine for Asthma?). Presented by DR. SAMUEL AYRES Jr.

The eruption began over twenty years ago following the long-continued administration of epinephrine for severe asthma. The patient states that the injections were given in the arm while she was in Honolulu and that the present eruption on the arm was preceded by hard "blue" sore lumps. The abnormality is confined to the left forearm and to a slight extent the upper part of the left arm. The posterior aspect of the arm shows apparent atrophy of the fat tissue. The entire forearm is diffusely swollen and indurated and feels heavier than the right arm. There is considerable thickening of the tissues over the point of the elbow. There are several small scars representing areas which had previously been ulcerated. A roentgenogram of the left forearm showed no abnormality.

DISCUSSION

DR. NELSON PAUL ANDERSON: This case is extraordinary. If the condition is a panniculitis, at least as far as the upper part of the arm is concerned, there is atrophy; in the forearm there is the opposite condition. I wonder if this patient received epinephrine in oil. I saw a woman who had had a number of injections of camphor in oil in her buttocks, and when she started moving around later she found large firm nodules, which were camphorated oil tumors which had gravitated down the leg. It is difficult to believe that a physician would give such injections in the forearm. They are usually given in the thigh. I think it would be worth while to take out one of the lesions; such a procedure would give the answer as to whether an oily vehicle had anything to do with it.

DR. SAMUEL AYRES JR.: When I first saw the woman the history was confused. I thought injections had been given in the forearm as well as in the upper part of the arm. I thought the condition was sensitivity to epinephrine; however, the appearance of the reaction is not anything like this; there are superficial abscesses and scars in cases of sensitivity to epinephrine. Dr. Anderson's suggestion may furnish the right answer.

A Case for Diagnosis (Discoid Lupus Erythematosus of the Tongue?).
Presented by DR. ARTHUR FLETCHER HALL.

N. P., a 73 year old white woman, states that in August 1941 she noticed for the first time a slightly thickened, pale, nontender patch on the right side of her tongue, which so far as she knows has not increased much in size or thickness but "has sometimes looked and felt different." She has had upper dentures since 1918 and lower since 1930. During the past few months a few pink scaly lesions have appeared behind her ears and on the inner aspects of the thighs. She states that during the past forty years she has had trouble with one ankle, affected with what has been diagnosed as "tuberculosis of the bone"; no diagnosis of pulmonary tuberculosis has ever been made. The right side and the right third of the dorsal surface of the tongue in its next to the distal quarter show a well demarcated pale plaque which is smooth and apparently fibrotic in the center. The borders are slightly elevated and smooth and show here and there just within their limits apparently altered papillae which are larger in diameter but not in elevation; these, at first glance, simulate plugged patulous follicle openings, as seen in lupus erythematosus of the glabrous skin.

Far back on the inner surfaces of the cheeks are scattered tiny lesions of Fordyce's disease. There are two small round erythematosquamous plaques posterior to the lobe of the right ear and several similar lesions on the inner aspects of the thighs. Histologic examination of tissue from the border of the lesion on the tongue was considered consistent with, but not typical of, lupus erythematosus.

DISCUSSION

DR. NELSON PAUL ANDERSON: I think this case is most interesting. I do not know what the disease is. The patient has some lesions on the body which are psoriasiform, and I feel that before one can make an absolute diagnosis of the lesion on the tongue one should have a biopsy of the lesions on the body. The microscopic section is not particularly characteristic of lupus erythematosus. There is a considerable inflammatory process scattered about the whole section.

DR. L. F. X. WILHELM: The patient presented a few lesions behind the right ear. I think if one of those lesions were examined histologically the picture would fit in with lupus erythematosus.

DR. FRANKLIN BALL: I saw other lesions besides that on the tongue. Why could not a double diagnosis be made in this case? The lesion on the tongue is the picture one would expect in lupus erythematosus of the tongue.

DR. SAMUEL AYRES JR.: I thought of the possibility of lichen planus. The lesion on the tongue certainly is not altogether typical, but there is something about the border that is suggestive. There are lesions on her lips that suggest lichen planus. She has a lesion on her thigh that could be circinate lichen planus. Further biopsies would be helpful.

DR. ARTHUR FLETCHER HALL: In view of the appearance of the lesion on the tongue and the history of probable tuberculosis of the bone in the ankle region, I think lupus erythematosus is the most likely diagnosis. The lesions behind the ear and on the thighs, which she called to my attention tonight for the first time, might help to clarify the diagnosis.

NOTE.—Histologic observations of tissue removed from the border of one of the lesions on the thigh were considered diagnostic of lichen planus. After twelve weekly injections of bismuth subsalicylate, 0.13 Gm. each, the lingual lesion healed, leaving a pale pliable scar, whereas the cutaneous lesions showed only partial improvement; these improved further after six fractional doses of unfiltered roentgen rays.

A Case for Diagnosis (Superficial Epitheliomatosis?). Presented by Dr. Walter F. Schwartz.

D. S., a 70 year old white woman has had the present eruption on the right cheek for thirty years. She was born in southern Germany and came to this country at the age of 6 months. In the beginning there were several discrete poorly defined scaling patches, but these have coalesced to form one large patch. There has been no tendency toward remission; in the past three years the lesion has grown a little faster. Burning and itching are the chief symptoms. Involving almost all of the posterior half of the right cheek and extending into the margins of the scalp in places where there is no loss of hair is a dusky red diffuse patch with a moderate amount of loose coarse scaling. The surface is not nodular, but in places there are small areas which have an apple jelly appearance on diascopic pressure, whereas most of the lesion blanches well with pressure. The margins are flat and indefinite. The patient's health is otherwise good, and there is no apparent involvement of the regional lymph nodes. Two biopsies on Sept. 30, 1941 showed essentially the some changes: There was no evidence of tuberculosis. The most important observation in the sections was a diffuse process involving the epidermis of nearly the entire surface. The epidermis showed diffuse thickening with formation of numerous blunt rete pegs. Throughout the entire thickness of the epidermis there was jumbling of the cells, which had largely lost their polarity. There was considerable variation in the size and shape of the cells, and intense hyperchromatism of the nuclei was found. Fairly numerous mitotic figures were present. In no place was there conclusive evidence of invasion of the basal layer. About the tips of the rete pegs there was an extensive infiltration of round cells; a few plasma cells and an occasional polymorphonuclear leukocyte were seen.

DISCUSSION

Dr. Saul Robinson: I should consider in this case a diagnosis of lupus erythematosus or sarcoid.

Dr. T. W. Nisbet: I first saw this patient in my office two years ago. My diagnosis at that time was lupus erythematosus of the Senear-Usher type. The lesion was impetiginous and crusted. I gave the patient a series of injections of a bismuth compound, and the condition improved greatly but did not heal completely.

Dr. Clement E. Counter: This case presents quite a problem in therapy. If the lesion is a true intraepidermal epithelioma it will not easily respond to radiation and it will have to be removed surgically. In a woman of this age such surgical intervention is not desirable. She has had the eruption so long that she will probably live on and not be bothered.

Dr. M. E. Obermayer: The histologic picture in this case is interesting, as it showed the typical features of intraepidermal carcinoma. It is not my experience that lesions of that type are radioresistant. It may well be that their alleged resistance to roentgen rays can be explained by the antiquated method of therapy in the form of small fractional doses. I should give this patient from 3,000 to 4,000 r, either in one sitting or divided into two doses at two or three days' interval; I believe that then the lesion would heal promptly.

Dr. Harry P. Jacobson: This patient has obviously a psoriasiform epithelioma of the face of long duration and involving an extensive area. The indicated treatment of this type of accessible epithelioma is the same as that governing cancer in any other location, that is, destruction of the malignant process. Roentgen irradiation should be given a thorough trial. Should this attempt at therapy prove insufficient, excision of the carcinomatous area together with a margin of normal skin by means of cautery should be resorted to, with the patient under general anesthesia. I cannot agree with the views expressed by some of the colleagues that the age of the patient and the fairly extensive area of involvement are contraindications to active radical treatment. No accessible malignant neoplasm in a patient of fairly good physical condition should be left untreated for reasons of postoperative destructive scarring; nor would I subscribe to the suggested method

of treatment by the presenter, to cauterize the involved area in piecemeal fashion. This, I believe, is a bad method of treatment.

DR. CHARLES CASKEY: I think one should not treat the disease apart from the patient. I should not give 3,000 r of roentgen rays.

DR. WALTER F. SCHWARTZ: I am the fifteenth or sixteenth physician who has seen this patient, and if I do not cure her she will go to some one else. It is true that she has a definitely malignant lesion now; whether to treat it now or not is apparently debatable. What was this lesion twenty years ago? Was it lupus erythematosus or benign superficial epithelioma? If it was the latter it simplifies treatment; if not, that would alter the therapy side. I believe that the type of therapy I am going to lean toward is superficial cautery.

A Case for Diagnosis (Tinea Versicolor?). Presented by DR. IRVING BANCROFT.

R. G., a 23 year old single woman, states that the onset of her present eruption was two years ago and it involved the arms. She now shows many small closely packed nonpruritic noninflammatory papules on the outer surfaces of the arms and on the back of the neck. On the chest there is a thickened area which formerly itched. There are several small areas of alopecia in the scalp; the hair started to fall at the time of the onset of the eruption. Microscopic examination of scrapings from several areas showed mycotic threads which were classified as atypical tinea versicolor.

DISCUSSION

PROFESSOR PLUNKETT (by invitation): The part that interested me was that the scrapings showed a picture which was typical of the rare Lewis and Hopper type of tinea versicolor. I cannot see the connection between the tinea versicolor and the falling hair.

DR. PAUL D. FOSTER: I saw the patient about a year ago. Her condition was considerably worse then than it is now. The lesion on her chest looked different, having hard spinous processes suggestive of Darier's disease, and all the lesions showed more discoloration than they do now. The biopsy was suggestive of Darier's disease. I did not look for fungi.

DR. CHARLES CASKEY: Maybe the finding of tinea versicolor was coincidental. It is on many skins normally.

DR. ARTHUR FLETCHER HALL: I thought the lesions on the nucha were definitely suggestive of Darier's disease.

DR. HARRY P. JACOBSON: The eruption presented by this patient is somewhat unusual as regards location though rather suggestive morphologically. It is essentially a follicular-papular dermatitis involving especially the back of the neck and is associated with little or no inflammatory interfollicular reaction but with a moderate degree of pruritus. The diagnosis of tinea versicolor, a saprophytic fungous infection usually characterized by absence of inflammatory cutaneous reaction, appears therefore untenable. The most likely diagnosis would appear to be either Fox-Fordyce disease or Darier's disease.

Multiple Benign Superficial Epitheliomas (Probably Arsenical); Psoriasis; Arsenical Keratoses. Presented by DR. SAMUEL AYRES JR.

J. S., a 56 year old Jew, has had psoriasis for over forty years. He states that he took arsenic (Asiatic) pills over a period of five years, the last time being about twenty-eight years ago. Plaques of a different type from his psoriasis began to develop about seven or eight years ago. Scattered over the trunk and right arm are a number of erythematous, scaly plaques with rather well defined borders, in places showing slight pearly nodular appearance. Some of the lesions show excoriation and crusting. Scattered over the palms and soles are large numbers of punctate keratoses, some of which are almost as large as a small pea and many of which are definitely elevated. There are remnants of a number of psoriatic lesions, especially on the elbows.

Multiple Benign Superficial Epitheliomatosis. Presented by DR. NELSON PAUL ANDERSON.

N. H., a 47 year old white woman, has noted multiple dry scaly lesions on the trunk for the past three or four years. None of the original lesions has disappeared, and several new ones have developed. There is a history of ingestion of arsenic about twenty years previously. At present she shows a typical flat nodular pea-sized basal cell epithelioma on the upper posterior aspect of the left shoulder and a half-dollar-sized but rather square scaly eczematous type of superficial epithelioma on the lateral aspect of the left hip in the region of the greater trochanter. The palms show no arsenical keratoses, but there are one or two small pinhead–sized lesions on the soles.

DISCUSSION OF TWO CASES OF MULTIPLE BENIGN SUPERFICIAL EPITHELIOMA

DR. HARRY P. JACOBSON: These cases should serve to remind one of the hazards involved in prescribing solution of potassium arsenite U. S. P. indiscriminately and permitting patients to take this drug for an extended length of time.

DR. CHARLES CASKEY: One should put on the prescription "Not to be refilled."

DR. NELSON PAUL ANDERSON: It is interesting to note the contrast that occurs in these patients. One took tremendous amounts of arsenic and presents many lesions, while the other patient took a little arsenic and shows few lesions. Both have superficial epitheliomas, one to a mild degree and the other to a decided degree.

DR. SAMUEL AYRES JR.: I think cases like these are far more common than is appreciated. They substantiate the report that Dr. Anderson first made in drawing attention to superficial epitheliomas and keratoses. Most lesions of this kind are multiple benign but sometimes run into squamous cell type, especially on the hands.

Epidermolysis Bullosa (Dystrophic Form). Presented by DR. NELSON PAUL ANDERSON.

E. B., a 34 year old white man, began to have blisters on his skin from slight trauma soon after birth and has continued to have such blisters from trauma ever since. At times the blister contents are watery and at other times hemorrhagic. No treatment has been of any benefit except exposure to sunshine. There is at present complete absence of finger nails and toe nails. There are atrophic changes in the skin on the sides and back of the neck, in the intergluteal region and in the lumbodorsal region of the back. In addition to the smooth shiny atrophic changes of the skin in these areas numerous superficial ulcerations of the skin are present. Leukoplakic changes are present on the buccal mucosa. An epithelioma is present on the left side of the tongue.

Lichen Planus of the Soles. DR. WALTER F. SCHWARTZ.

S. G., a 36 year old Negro gardener, states that about two months ago lesions first appeared on the forearms, legs and glans penis and both soles. At first there was little or no itching, but in the past three weeks it has become severe. The plantar lesions do not itch. There is no history of nervous tension, shock or worry. On the instep of each foot is a group of fifteen or twenty firm keratotic papules without redness; the individual lesions are almost cone-shaped hyperkeratoses. These groups of lesions extend medially on to the side of the foot where there is no pressure from the shoe. There are no similar lesions on the palms. There are six or eight hypertrophic lesions of lichen planus on the legs, and on the forearms are several typical lichen planus papules. There are also discrete and confluent annular whitish lesions on the lips and glans penis. He has received five weekly injections of thio-bismol, 0.2 Gm., with intensification of the itching.

DISCUSSION

DR. PAUL D. FOSTER: I thought the patient had typical lichen planus.

DR. ARTHUR FLETCHER HALL: This is the first example I have seen of hypertrophic lichen planus on the penis; the patient has several verrucous lesions there and several on his arms.

DR. M. J. WOLFF: I think this patient's condition falls in the classification of lichen planus obtusus et corneus.

Lupus Erythematosus and Raynaud's Disease. Presented by DR. KENDAL FROST.

Mrs. J. M., a 21 year old white woman, states that she has an aunt who has a circulatory disturbance of her hands and feet and a niece whose hands turn white on exposure to cold. As long as she can remember she has had trouble with the circulation in her hands and feet. When exposed to cold they turn white. The nail of her left index finger was removed five years ago and has not regrown normally. She also had a sore on the tip of this finger which was slow in healing. When first seen on Dec. 9, 1941, she complained of an eruption on the face which had been present four months. It began with a small spot, and other spots appeared in succession. There have been no subjective symptoms. She has for some time had a sore on the tip of the right index finger.

She is a well nourished, healthy-appearing young woman. On her cheeks and behind her ears there are several oval and circinate lesions measuring 10 to 20 mm. in diameter. These are atrophic in the centers, while the margins are erythematous and telangiectatic with slight scaling. The hands are cool. When seen immediately after exposure to cold the fingers are waxy white; after she has been in a warm room for a few minutes they become bluish. Both index fingers are slightly tapered at the distal phalanges, and the nails of these two fingers are curved longitudinally. On the tip of the right forefinger is a small deep crust.

A blood count showed 5,420,000 red cells and 19,050 white cells, with polymorphonuclear leukocytes 67 per cent, lymphocytes 19 per cent, mononuclear leukocytes 8 per cent and eosinophils 6 per cent. The hemoglobin content was 95 per cent.

The lesions on the face have shown definite improvement after six weekly intravenous injections of gold sodium thiosulfate, 10 to 25 mg. each.

Palmar Lesions (Syphilis Corné?). Presented by DR. BEN A. NEWMAN.

An approximately 35 year old man had secondary syphilis with a positive Wassermann reaction of the blood in August 1930. His treatment schedule was as follows: August to October 1930, ten injections of neoarsphenamine; November 1930 to March 1932, no treatment, and April 1932 to December 1933, about forty injections of a bismuth compound. In January 1934 the results of examination of the spinal fluid were positive (details not known), but there were no signs or symptoms of neurosyphilis. From January 1934 to January 1936 sixty-five injections of tryparsamide and fever therapy were given. The spinal fluid and the cell count were normal. The Wassermann reaction of the blood was positive. From February to November 1940 twenty-five injections of tryparsamide were given. Four examinations of the spinal fluid between 1935 and 1940 all gave negative results. Tests of the blood for syphilis constantly showed positive reactions.

Since 1936 he has had a recurrent eruption on the right palm and right sole. The remissions of this eruption were apparently unrelated to treatment. At this time he presents scattered match head–sized to split pea–sized lesions on the right palm and flexor surfaces of the fingers. The lesions vary in color from dull red to dull brown and flesh color. Some of the lesions are flat macules; others are firm keratotic infiltrated plugs, and still others are scaly spots.

DISCUSSION

DR. SAUL ROBINSON: I suggest that this patient receive a course of arsphenamine if the lesions are resistant to therapy.

DR. SAMUEL AYRES JR.: I suggest a microscopic examination to see if there is any fungous infection. Some of the lesions on the foot looked like a fungous infection, and the lesions on the hand suggested an id.

DR. CLEMENT E. COUNTER: Several months ago I presented a patient with palmar lesions who had syphilis. The biopsy showed palmar psoriasis in spite of absence of other evidence of psoriasis at the time. These lesions do not need to be due to syphilis simply because the patient is being treated for a long-standing syphilis. A biopsy would be of value.

DR. BEN A. NEWMAN: The patient is very intellectual. The disease started when he was in college and has been treated in various universities by well known dermatologists. Two weeks ago, from the lesions on the palms my first impression was angioneurotic recurrence; further history, however, discloses that he has been free of neurosyphilis for years. This evening most of the annular lesions have disappeared; most of the lesions are keratotic. The eruption looks like arsenical keratosis or palmar syphilid. He has had tryparsamide, bismuth and little arsphenamine. The serologic reaction of his blood has been positive ever since ten years ago.

NOTE.—The palmar lesions disappeared after three injections of 0.6 Gm. of neoarsphenamine.

Melanotic Nevus. Presented by DR. NELSON PAUL ANDERSON.

D. A. W., a 2 month old white boy, presents a large pea–sized flat coal black pigmented nevus on the right side of the trunk. His mother first noted a pigmented spot on the right side of the trunk about two weeks after his birth. The lesion seems to be getting larger but possibly not in any greater degree than the child is.

DISCUSSION

DR. NELSON PAUL ANDERSON: I think the lesion ought to be removed widely and deeply. Unfortunately I am not particularly qualified to know how much procaine hydrochloride and how much shock a child of this age can stand. I think this is the youngest patient I have ever seen with a melanotic nevus. There are at present between 2 and 4 cases on record in which children have been born with metastatic melanomas which have passed through the placenta. The mother in this case has no moles on her body.

DR. HARRY P. JACOBSEN: I am grateful to Dr. Anderson for his reference to the literature about the transmission of melanotic growths through the placenta. About a year or so ago in the malignant tumor service at the Los Angeles County Hospital there was a pregnant woman with widespread metastases to the chest and other parts of the body from a malignant melanoma of the face. She died shortly after entering the hospital, and a postmortem cesarean section was performed with the recovery of a dead infant. Autopsy of the latter showed no evidence of transmitted melanoma.

The therapeutic problem presented by Dr. Anderson's little patient is a serious one. Assuming that treatment is indicated, it would appear that this should be as radical as possible. My own preference is radical cautery excision with the patient under suitable general anesthesia. The excision should include a fair margin of normal-appearing skin and should extend to a sufficient depth to include most of the soft tissues. The youngest patient that I operated on for a highly malignant tumor of the face was a 3 week old infant, who had been treated by another colleague with solid carbon dioxide about a week after birth, under which treatment the growth flared and grew rapidly to large dimensions. The microscopic structure of this lesion was that of a highly malignant angio-endothelioma. Incidentally, I might state that while the cautery excision involved approximately one third of the face, the resulting scar is pliable and not at all unsightly.

A Case for Diagnosis (Verrucae with Lichen Planus?). Presented by DR. CHRIS HALLORAN.

Mrs. C. K. C., a 30 year old white woman, was treated for lichen planus by fractional weekly roentgen therapy from July to September 1941. When she was first seen, on July 12, there were typical lesions of lichen planus on the arms, hands and leg. There is now a marble-sized verrucous lesion on the lateral aspect of the right leg in a plaque that was formarly a lesion of lichen planus. This lesion has not responded to treatment but has continued to grow in size. Within the past few months a pea-sized lesion has developed lateral to the external canthus; this lesion is violaceous in color, but the raised border suggests epithelioma. The lichen planus lesions cleared with fractional roentgen treatments, but the verrucous lesion remained unchanged. The new lesion on the left cheek developed two months after the lichen planus cleared.

DISCUSSION

DR. SAUL ROBINSON: I think that the patient probably has a basal cell epithelioma on the cheek; the other lesions look like lichen planus.

DR. ANKER K. JENSEN: I believe the patient has a verruca in the area of lichen planus. Her daughter has a number of verrucae. I think this case is one of infection by contact.

DR. NELSON PAUL ANDERSON: I think the whole picture is lichen planus.

DR. CHRIS HALLORAN: I presented this case because of the verrucous lesions developing on plaques that were clinically typical lichen planus. With weekly roentgen treatments the generalized lichen planus cleared but the verrucae continued to grow. The lesion on the cheek looks like an early epithelioma. However, it is violaceous.

Tinea Capitis with Trichophytid. Presented by DR. THOMAS W. NISBET.

L. B., a 5 year old white girl, has had in her scalp scaly, crusted circinate lesions pierced by broken hairs for the past four months, while a generalized eruption of circinate tinea-like lesions have been scattered over the face and trunk for one month. When the patient was first seen, on Dec. 4, 1941, she presented several scaly crusted circinate lesions of the scalp in which many broken hairs were present. There was also a generalized eruption consisting of circinate tinea-like lesions scattered over the trunk and face.

Direct microscopic examination of scales and hairs (macerated in 20 per cent potassium hydroxide) from the lesion on the scalp shows large numbers of spores and fragments of mycelial filaments. Similar examination and cultures of scales from the neck and lesions on the trunk revealed no fungi. An epilating dose of roentgen rays was administered on December 6; epilation was complete on December 23. The lesions on the trunk at first received active fungicidal treatment, but as no results other than dermatitis venenata were obtained and laboratory examinations revealed no fungi present in these lesions this treatment was stopped.

DISCUSSION

DR. M. J. WOLFF: I do not believe I could make a diagnosis of tinea at present, since the scalp is epilated. The lesions on the body may be trichophytid.

DR. CHARLES CASKEY: Was the causative organism identified?

DR. ARTHUR FLETCHER HALL: I think that the lesions on the trunk are definitely follicular and aggregated into plaques. I consider this a classic case that would have done Sabouraud's heart good.

DR. THOMAS W. NISBET: My original impression was that the patient had the small spore type of tinea capitis. The hairs were loaded with the fungi. The original lesions on the trunk were follicular.

SAN FRANCISCO AND LOS ANGELES DERMATOLOGICAL SOCIETIES

DR. ARNE E. INGELS, M.D., *Chairman*

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Joint Meeting, San Francisco, May 2, 1942

Lupus Erythematosus. Presented by DR. FREDERICK G. NOVY JR., Oakland, Calif.

G. R., a 20 year old Italian laborer, was first seen in the University of California dermatologic clinic on April 21, 1942. Six months previously he had received 2 Gm. of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) daily for one week for a gonorrheal urethritis. This condition improved but recurred two weeks later. At the same time an eruption appeared on his face and then on his hands. The feet later became involved. He has lost 15 to 20 pounds (7 to 9 Kg.). He also complains of weakness and general malaise. His oral temperature has been as high as 38 C. (100.4 F.). Pain has been present between the shoulders and in the elbows.

A general physical examination revealed evidence of illness and malaise. There were signs of pleural thickening at the base of the left lung. A rough systolic murmur could be heard over the entire precordium. There was some tenderness over the liver, and the spleen was barely palpable. Cutaneous changes included a dusky erythematous scaly maculopapular and telangiectatic eruption on his face, ears, scalp, hands, elbows, legs and feet. A generalized lymphadenopathy was noted. Herpetiform shallow ulcerations have appeared on his hard palate more recently.

Urinalysis showed a heavy trace of albumin, 10 to 15 pus cells, 6 to 8 erythrocytes and an occasional coarsely granular cast per dry field with high magnification. The hemoglobin content of the blood was 82 per cent. The blood count revealed 3,870,000 erythrocytes and 6,000 leukocytes. The differential count showed 68 per cent filamented neutrophils, 4 per cent nonfilamented cells and 2 per cent lymphocytes. The sedimentation rate was 24 mm. in twenty minutes. The Wassermann and Kahn reactions were negative. A roentgen examination showed a pleural effusion on the left side.

Treatment was started on April 27 and included the administration of a polyvitamin compound and 2 units of crude liver extract intramuscularly daily.

Lupus Erythematosus, Tuberculosis and Chrysiasis. Presented by DR. HARRY E. ALDERSON, San Francisco.

O. B., a 36 year old white housewife, presents typical scars of lupus erythematosus in a "bat wing" distribution. In addition, there is extensive blackish discoloration of her forehead and infraorbital areas. There remains a small active lesion of lupus erythematosus at the mucocutaneous border of her upper lip.

In January 1936 swelling and redness of her cheeks and nose developed. This subsided but recurred six months later in conjunction with a "streptococcic sore throat." She was given 40 grains (2.6 Gm.) of sulfanilamide daily in conjunction with a liver preparation. This resulted in temporary improvement. Several dermatologists were consulted, and she was treated with weekly injections of 30 to 50 mg. of gold sodium thiosulfate intermittently for two years.

A general physical examination revealed no abnormalities.

A roentgen examination of the chest revealed increased bronchial markings and a questionable apical scar. The urine and sputum were normal. Multiple blood counts performed on various dates demonstrated a mild anemia and a slight leukocytosis with a normal differential count.

An infected tooth was extracted. A culture of material from this tooth revealed many alpha and a few gamma hemolytic streptococci. A vaccine has been made from this material.

Lupus Erythematosus, Erythema Induratum and Sclerodactylia. Presented by DR. HARRY E. ALDERSON and DR. CHARLES ALBERT SHUMATE, San Francisco.

D. R., a 30 year old Mexican woman, was first seen on Feb. 19, 1942. When she was 11 years old an erythematous atrophic lesion developed on her nose and cheeks in the typical butterfly distribution. The lesions subsided under treatment with gold sodium thiosulfate and, later, a bismuth compound administered by Dr. Merlin Maynard. When she was 18 the fingers of both hands became painful and reddened. The right fifth finger was removed because of gangrene. Since then the pain has subsided but the fingers have become progressively more sclerodermatous. In February 1942 an eruption developed on her right foot consisting of pustules and vesicles.

The patient also presents scattered areas of depigmentation. She has had recurrent nodules on her legs for the past eighteen years. These undergo necrosis and ulceration.

Roentgen examination of her chest shows bronchiectasis and possible pulmonary tuberculosis. Her hands show neurotrophic changes in the distal phalanges suggesting scleroderma.

The Wassermann reactions of the blood and spinal fluid were negative. Blood counts and urinalyses showed no abnormalities. Histologic examination of material from the face (the nose), reported by Dr. Arne E. Ingels, showed features compatible with lupus erythematosus, but sections of material from the face and hand were more suggestive of scleroderma or possibly of Raynaud's disease.

DISCUSSION OF CASES OF LUPUS ERYTHEMATOSUS

DR. FRANKLIN I. BALL, Los Angeles: These cases are distinctive instances of the diagnoses as presented. I appreciate observing the case of Dr. Alderson in which the focus of infection was found and eliminated. I believe that focal infection is the cause in many cases. Yet it is difficult to achieve the results obtained in that case.

DR. C. JULIAN LUNSFORD, Oakland, Calif: Dr. Templeton and I had an interesting case of disseminated lupus erythematosus seven or eight years ago. A dentist pulled out all of the patient's teeth and the previously discoid eruption became disseminated. Streptococcus viridans was cultured from the teeth. Desensitization with a vaccine gave good results.

DR. HIRAM D. NEWTON, San Diego, Calif.: I recently treated a patient with lupus erythematosus with sulfathiazole. The eruption responded at first but promptly recurred on cessation of administration of the drug. The next time the drug was given the eruption did not respond. However, it is responding to the administration of liver extract.

DR. STUART C. WAY, San Francisco: I have a patient with disseminated lupus erythematosus at present. I was treating her with a preparation of arsenic and bismuth. Pneumonia developed and the attending physician prescribed sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine). Treatment with this drug resulted in decided improvement.

DR. HIRAM E. MILLER, San Francisco: The patient with lupus erythematosus disseminatus presented by Dr. Novy is of interest in regard to his response to sulfathiazole. He dates the onset of his disease to sulfathiazole treatment for acute gonorrhea. In many patients this disease is precipitated by such factors as sunburn and insect bites. Perhaps sulfathiazole could photosensitize the skin. It may have been the "trigger mechanism" precipitating the eruption just at the time when the disease was on the threshold of developing.

DR. HARRY C. L. LINDSAY, Pasadena, Calif.: About a year ago a report of a case of lupus erythematosus of twelve years' duration was published in which

the eruption subsided after treatment with sulfanilamide (*Urol. & Cutan. Rev.* **45**:462 [July] 1941). An eruption due to sulfanilamide developed after a dosage of only 40 grains (2.56 Gm.) per day. However, when this eruption cleared the lupus erythematosus also disappeared.

DR. NORMAN N. EPSTEIN, San Francisco: In the administration of sulfonamide drugs to patients with disseminated lupus erythematosus, the question might be raised whether a person who has a leukopenia can be given these drugs safely. I think it is safe to give them.

DR. MERLIN T. R. MAYNARD, San Jose, Calif.: I have been following the third patient for the past eighteen years. Although she states that she is Mexican, she is definitely Negroid. When I first saw her, she presented a hypertrophic lupus erythematosus of the face. During the next six years lupus erythematosus developed also in her sister, which cleared with gold sodium thiosulfate therapy. At the age of 18 the patient was seen with papulonecrotic tuberculids. The Wassermann reaction was negative. Roentgenographic examination of the chest showed changes interpreted as possible interstitial tuberculosis. When seen four years later, she presented both erythema induratum and sclerodactylia. I last saw her a month ago with gangrene of a toe. I feel that the history is worth repeating because of the variety of tuberculids she has had and because of the development of the sclerodactylia. It is interesting that her sister had lupus erythematosus at approximately the same age. The patient states that in a maternal aunt pains in the legs and blueness of the toes are developing.

DR. FREDERICK G. NOVY JR., Oakland, Calif.: G. R. presents all of the classic features of disseminated lupus erythematosus. The only unusual feature is the patient's sex. He has some cardiac changes, and possibly autopsy will reveal an endocarditis of the Libman-Sachs type.

DR. HARRY E. ALDERSON, San Francisco: Dr. Maynard has given us a good résumé of the case of D. R. The various lesions are fairly typical of the diseases mentioned. The appearance of the hands and feet suggests scleroderma, although not definitely. I feel that the eruption on the face is lupus erythematosus.

Xanthoma Tuberosum Multiplex. Presented by DR. STUART C. WAY, San Francisco.

A. S., a 31 year old white man, first noted cutaneous lesions on the extensor surfaces of his elbows five years ago. Since then the buttocks, palms and soles have become involved. One brother is similarly affected.

The patient presents an eruption in the aforementioned locations consisting of yellowish and pink papules and nodules.

Histologic examination confirmed the diagnosis as presented.

A blood count and a urinalysis gave normal results. The cholesterol content of the blood was 145.4 mg. per hundred cubic centimeters, the sugar content 83.6 mg. and the urea content 24.6 mg. The bleeding time was nine minutes, the capillary coagulation time four minutes, the icterus index 24 and the reactions to the van den Bergh and Kolmer tests negative.

Xanthomatosis. Presented by DR. FRANCES A. TORREY, San Francisco.

E. M., a 49 year old white man, was first seen in the University of California dermatologic clinic on April 18, 1942. The patient was well until two years ago, when nodules developed on the hands, back and elsewhere. A tentative diagnosis of hypothyroidism with myxedema and xanthomatosis was made. The urine was normal except for a very faint trace of albumin.

A blood count was also normal. The plasma cholesterol was 926 mg. per hundred cubic centimeters. The serum was creamy. The basal metabolic rate was —35 per cent. The reaction to a test for carotene in the blood was positive.

A Case for Diagnosis (Xanthoma?). Presented by Dr. Charles Albert Shumate, San Francisco.

M. C., a 2½ year old boy, was seen for the first time today at the clinic of St. Mary's Hospital. When he was 6 months old yellow and brown papules appeared on his neck. These gradually spread until now they are scattered profusely over his face, trunk and extremities. His hands and feet are unaffected.

The lesions are small elevated papules and nodules. Under diascopic pressure they appear as yellowish xanthomatous lesions.

His general health is good. There is no history of cutaneous diseases in other members of his family.

DISCUSSION OF CASES OF XANTHOMATOSIS

Dr. Harry C. L. Lindsay, Pasadena, Calif.: I feel that the boy, M. C., has urticaria pigmentosa because irritation of some of the papules showed that they have erectile capacity.

Dr. Nelson Paul Anderson, Los Angeles: I suggest a diagnosis of nevoxanthoendothelioma for M. C. I do not believe that this diagnosis can be substantiated without further study. However, xanthomas beginning at the age of 6 months suggest this diagnosis.

There is no question about Dr. Way's case of xanthoma tuberosum multiplex. If he would tell me how to cure this condition I should consider my trip well spent.

The patient with diabetic xanthoma presents not only diabetes and apparently diabetic xanthoma but also carotenemia. If the problem of xanthoma is ever to be solved, it will be by studies in cases like this. There is some connection between diabetes and carotenemia. Diabetes is more than a disturbance of the carbohydrate metabolism; changes in fat metabolism are also present. There is certainly some relationship between carotenemia and thyroid dysfunction.

Dr. Frank H. Stibbens, Oakland, Calif.: I saw E. M. previously. At that time he presented both xanthomas and myxedema. Both responded to thyroid therapy. As soon as he discontinued taking thyroid the xanthomas recurred.

Dr. Stuart C. Way, San Francisco: The results of chemical examination of the blood of A. S. were disappointing. The normal cholesterol value suggests that the disease may be due to inability of the affected cell itself to eliminate lipids rather than to an increase of lipids in the blood stream. The clinical and histologic pictures were typical of xanthoma tuberosum multiplex.

Keratosis Follicularis. Presented by Dr. Norman N. Epstein and Dr. Frances Keddie (by invitation), San Francisco.

E. N., a 30 year old white woman, is presented from the clinic of Mount Zion Hospital with an eruption of nineteen years' duration. She presents discrete and coalescent keratotic follicular papules on the scalp, forehead, chest, back and dorsa of the hands.

She has received 30,000 U. S. P. units of vitamin A daily for the past ten days without any visible change.

Keratosis Follicularis. Presented by Dr. Arne E. Ingels, San Francisco.

A. G., a 21 year old white man, presents lesions involving his scalp, face, neck, trunk and arms. These consist of hyperkeratotic papules forming large deeply pigmented masses especially on the trunk. The lesions are noninflammatory.

The patient's father and grandmother have the same disease.

Histologic examination of tissue from the back was interpreted as showing keratosis follicularis.

DISCUSSION OF CASES OF KERATOSIS FOLLICULARIS

Dr. Kendal Frost, Los Angeles: A. G. had lesions on his gums and palms also. I wonder if the dose of 30,000 U. S. P. units of vitamin A for E. N. was correct. I doubt if this is enough to obtain much benefit.

DR. ARNE E. INGELS, San Francisco: A. G. is also being treated with vitamin A. Sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) is being applied locally to a limited area experimentally.

DR. STUART C. WAY, San Francisco: The histologic sections that I saw were not typical of keratosis follicularis. Although there was some vacuolation, I could not find any psorosperms. I examined the sections from only 1 case.

DR. NORMAN N. EPSTEIN, San Francisco: I should like to discuss the use of vitamin A in my case (E. N.). The dosage administered was selected on the recommendation of Dr. Fasal, who has done much experimental work on vitamin A deficiency in Malaya. He feels that true vitamin A deficiencies respond well to 10,000 U. S. P. units a day and that larger doses are unnecessary. I do not believe that there is any question about the diagnosis in either case.

Localized Scleroderma. Presented by DR. FRANCES TORREY, San Francisco.

L. W., a 68 year old white man, entered the University of California Clinics in 1940. At that time a double-furrowed scar running in a sagittal direction in the right frontal area was described. These furrows were approximately 7 cm. in length and 2 cm. apart. A dimple-like depression was first noted in this area about fifteen years ago. This gradually extended. A second parallel furrow developed seven or eight years later.

The patient presents an area of atrophy in the aforementioned location.

Localized Scleroderma. Presented by DR. FRANCES TORREY, San Francisco.

D. D., a 13 year old white schoolboy, entered the University of California Hospital on April 27, 1942. During the summer of 1941 he was severely sunburned. After this, he noted that the skin of his right shoulder and arm had become depigmented and discolored. In October 1941 he was in an automobile accident but sustained no injury. Roentgenograms of the spine at that time showed no abnormalities. In December 1941 he fell on his right elbow but injured it only slightly. It seemed normal after a day or two. His general health has been excellent. In January 1942 his mother noted that he could not extend the fingers of his right hand completely. In February a physician noted some limitation of extension of his right elbow. There has never been any pain, swelling, tenderness or redness of this arm. Occasionally his right palm feels numb.

A general physical examination revealed no abnormalities except for those of the right shoulder and arm. The skin overlying the right shoulder and extending in a linear patchy distribution down the radial side of the arm is depigmented and partially atrophic. There are guttate peripheral satellite lesions. The involved areas are semi-indurated and nonpitting with a narrow bluish halo. The underlying muscles feel fibrous and are smaller than the corresponding muscles of the left side. There is a slight contracture of the three medial fingers of the right hand. Pronation, supination and shoulder abduction are somewhat restricted. The muscle power is good.

The urine, sedimentation rate, hemogram and results of tests for calcium, phosphorus, phosphatase and vitamin C were all within normal limits.

Roentgenographic examination of the right arm and hand revealed only mild osteoporosis.

Scleroderma (Progressive Type). Presented by DR. NORMAN N. EPSTEIN, San Francisco.

G. S., a 50 year old Italian, was first seen in the University of California dermatologic clinic on Nov. 25, 1941. Tightness and hardness of the skin had first appeared six years previously. The hands were involved first, but the process has spread to involve the trunk, right thigh and feet. The onset was not preceded by any febrile episode, muscle soreness or eruption.

The patient presents sclerodactylia with a bluish, waxy, erythematous cast to the involved skin. There is also some hyperpigmentation.

A general physical examination revealed no abnormalities. The urine and blood count were normal. The cholesterol content of the plasma was 88 mg. per hundred cubic centimeters. The basal metabolic rate was +8 per cent. The urinary creatinine was within normal limits, and there was no creatinuria. The vitamin C level was 0.27 mg. per hundred cubic centimeters.

Treatment has included administration of a pancreatic tissue extract and fever therapy. Neither of these has led to any improvement.

A histologic section shows changes compatible with those found in scleroderma.

DISCUSSION ON CASES OF SCLERODERMA

DR. NELSON PAUL ANDERSON, Los Angeles: L. W. presents the type of localized scleroderma that resembles a saber scar.

D. D., in my opinion, does not have true scleroderma. I grant that he has scleroderma-like changes, but I feel definitely that there is an underlying nerve injury. He certainly has had two injuries to his right arm, including a broken elbow and an automobile accident.

G. S. presents a classic picture of scleroderma of the progressive type.

DR. HIRAM E. MILLER, San Francisco: I agree with Dr. Anderson in regard to D. D. He has scleroderma-like changes and not true scleroderma. However, I cannot agree with the idea that it is due to a neural injury to the elbow or shoulder girdle. The process is already beginning on the other hand. There is definite atrophy of the palmar interosseous muscles. I think there is a cutaneous change secondary to some wasting neuromuscular disease.

DR. MERLIN T. R. MAYNARD, San Jose, Calif.: One cannot rule out the traumatic factor just because the eruption of D. D. is bilateral. If the injury were in the spine, the changes could be bilateral. I have seen scleroderma following the distribution of an old herpes zoster. This indicates that scleroderma-like changes can follow a nerve distribution.

DR. HIRAM D. NEWTON, San Diego, Calif.: Were any roentgenograms taken of the shoulder girdle? Dr. Graves suggested the possibility of a cervical rib.

DR. ARNE E. INGELS, San Francisco: It is difficult to diagnose scleroderma histologically in its earlier stages. However, the dermal appendages are present in the case of D. D., which is usually not the case in true scleroderma. There is definite atrophy of the epidermis and swelling of the collagen fibers. However, this is not as great as usually seen in scleroderma. To me, this suggests an atrophic rather than a sclerodermatous change.

DR. FRANCES TORREY, San Francisco: There were no roentgenologically apparent changes in the shoulder girdle. However, there was some calcification of the soft tissue. The most interesting feature has been the rapid progress of the process in D. D. I feel that the diagnosis in this case is localized scleroderma.

The roentgenogram of the skull of L. W. taken yesterday shows some calcification in the post-thalamic area. This might explain the nerve distribution in this case.

Raynaud's Disease with Sclerodactylia and Calcinosis Circumscripta. Presented by DR. JOHN GRAVES, San Francisco.

P. S., a 38 year old Italian housewife, has suffered from stiffness and coldness, chiefly of the hands, for the past sixteen years. In 1938 an ulcer appeared on the tip of the right index finger. Peripheral vascular studies demonstrated a decided reaction to cold. Immersion of a finger in moderately cold water induced blueness and pain, but there was no reaction of this type to low temperatures. Oscillometrographic readings were low in both arms. Vascular dilatation occurred after anesthesia, and the temperature of the fingers rose several degrees centigrade. There was no evidence of a cervical rib. Changes demonstrated by roentgen-

ography of the right hand were compatible with those of Raynaud's disease, including slight periarticular proliferation and destruction of the terminal phalanges. A gastrointestinal series confirmed a clinical impression of esophageal achalasia. In October 1941 she first noted some tender nodules in the soft tissue overlying the left knee.

Examination reveals partial sclerodactylia of the right hand with hardening and coldness of the skin. A scaly atrophic depression is present on the tip of the right index finger. There are several small firm tender nodules in the subcutaneous tissue over the left patella.

A Case for Diagnosis (Raynaud's Disease?). Presented by DR. HARRY J. TEMPLETON, DR. C. JULIAN LUNSFORD and DR. HERMAN V. ALLINGTON, Oakland, Calif.

R. W. P., a 41 year old white American man, consulted us in December 1941 because of necrosis of the tips of the left index finger, right index finger, right ring finger and left great toe. The patient stated that the process started twelve years ago on the toe. Eight years ago the lesions healed, but they recurred one and one-half years ago. The involved fingers are painful and tender, but this is relieved by application of a 4 per cent phenol ointment.

The entire end of each exposed digit is deeply ulcerated exposing the underlying phalanx. Although the fingers do not show the typical pallor of Raynaud's disease, there has been a suggestion of such changes in the past.

The patient is receiving injections of pancreatic tissue extract three times a week. The dosage has varied from 1 to 3 cc. per injection.

The urine and the blood count were essentially normal. The reaction to a Kline test was negative.

Acrodermatitis Chronica Atrophicans. Presented by DR. HIRAM E. MILLER, San Francisco.

Mrs. J. M., a 65 year old housewife, born in Germany, has had an eruption involving the legs and dorsa of the feet for fifteen years.

She presents diffuse atrophy with prominent veins, telangiectasia and scaling in the aforementioned locations. There are a few scleroderma-like plaques and bands in the region of the knees. An ulcer is present over the left medial malleolus.

Urinalysis revealed a few erythrocytes and granular casts in the sediment. A blood count was normal. The basal metabolic rate was +5 per cent. The cholesterol content of the blood was 222 mg. per hundred cubic centimeters and the vitamin C level 1.10 mg.

DISCUSSION OF CASES OF RAYNAUD'S DISEASE AND ACRODERMATITIS CHRONICA ATROPHICANS

DR. ANKER K. JENSEN, Los Angeles: I should appreciate further discussion on the treatment of scleroderma. One patient of mine showed 80 per cent improvement with iontophoresis with mecholyl chloride (acetylbetamethylcholine chloride). I have also seen patients improve with the use of pancreatic tissue extract.

DR. STUART C. WAY, San Francisco: Dr. Charles Dennie has treated a number of patients with hot baths with good results. I have used this for 2 patients along with infra-red irradiation with considerable progress.

DR. NORMAN N. EPSTEIN, San Francisco: G. S., the patient with progressive scleroderma presented earlier today, was treated with artificial hyperpyrexia. It was felt that this might improve the circulation to the skin in this manner. However, it did not seem particularly beneficial in this instance.

DR. ERVIN EPSTEIN, Oakland, Calif.: Dr. Allington and I treated 2 patients with generalized scleroderma with pancreatic tissue extract for two and one-half years. Both patients showed improvement for the first three or four months, but

then the process became stationary. I have also treated 4 patients with fever therapy and 2 showed decided improvement. In another instance the use of a passive vascular exercising machine resulted in marked improvement in the extremities.

DR. MERLIN T. R. MAYNARD, San Jose, Calif.: I have been particularly interested in the use of vitamin D to remove the calcium from the skin of patients with scleroderma. Of course, this can be accomplished by other means, such as the use of ammonium chloride, ascorbic acid and fever therapy. All of these modalities will help patients with this condition if the calcium intake is decreased at the same time. I have treated only 4 patients with localized scleroderma with vitamin D. Moderate doses of 60,000 to 80,000 U. S. P. units a day should be given and continued for long periods. One cannot get results in six weeks.

DR. CHARLES ALBERT SHUMATE, San Francisco: At the last meeting of the San Francisco Dermatological Society I presented a child with scleroderma whose basal metabolic rate was —26 per cent. This patient was given thyroid and appears to be completely well at present. Another child, presented before the San Francisco Dermatological Society (ARCH. DERMAT. & SYPH. **44**:311 [Aug.] 1941), has been given thyroid, an insulin-free extract of pancreas, etc., without benefit. Her basal metabolic rate has always been within normal limits.

DR. PAUL D. FOSTER, Los Angeles: I treated 2 patients with generalized scleroderma with fever therapy. In both the condition improved but became worse later.

DR. HARRY C. L. LINDSAY, Pasadena, Calif.: I obtained a 30 per cent improvement in 1 patient with acrodermatitis chronica atrophicans by the administration of large doses of nicotinic acid.

DR. FRANCES TORREY, San Francisco: One point well demonstrated by today's discussion and by a review of the literature is that most small series show 50 per cent good results. This is independent of the type of therapy employed. Perhaps half of the patients do well regardless of therapy.

DR. HARRY E. ALDERSON, San Francisco: In 1 case of acrodermatitis chronica atrophicans at Stanford Dr. Reichert injected alcohol intraneurally, with decided improvement in the cutaneous condition.

Lichen Sclerosus et Atrophicans. Presented by DR. ARNE E. INGELS, San Francisco.

L. M. H., a 56 year old white housewife, presents an eruption consisting of gray and white angular lesions, 2 to 3 mm. in diameter, with an atrophic depressed appearance and with a central horny plug. The lesions involve her breasts and extend upward to involve the neck and inferiorally to the abdomen, inguinal region and thighs. None of the lesions presents the induration of scleroderma. In many regions confluence has led to the development of large lesions. These areas are covered by a thin atrophic epidermis showing "cigaret-paper-like wrinkling."

Histologic examination shows changes consistent with lichen sclerosus et atrophicans.

At present she has an extensive dermatitis venenata of her chest apparently due to a lotion containing tincture of benzoin and resorcinol monoacetate.

DISCUSSION

DR. JOHN GRAVES, San Francisco: The interesting feature is that the eruption followed a "streptococcic sore throat." The localized scleroderma and scleroderma-like lesions are not unusual.

DR. HARRY C. L. LINDSAY, Pasadena, Calif.: Wise reviewed the subject of "white spot disease" a number of years ago (*J. Cutan. Dis.* **32**:629, 1914). It is a very difficult subject to understand.

DR. ARNE E. INGELS, San Francisco: Such cases always raise considerable discussion as to the differentiation of this disease from scleroderma. In this case the central plugging both grossly and microscopically puts the eruption in the classification of lichen sclerosus et atrophicans. I am unable to state definitely whether this is a separate disease or a form of scleroderma.

Boeck's Sarcoid. Presented by DR. ARNE E. INGELS, San Francisco.

Miss L. C. had two small papular lesions in her nasal cavity two years ago. A biopsy by Dr. Russell Fletcher substantiated the diagnosis of sarcoid. After this the lesions disappeared but soon reappeared and formed an indurated tumor close to the medial concha.

The following methods of treatment have been used with varying degrees of benefit: application of solid carbon dioxide and roentgen rays, injections of a bismuth compound and administration of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) orally and lactic acid locally.

Reactions to tuberculin tests have been positive. Neither acid-fast bacilli nor spirochetes have been demonstrated in histologic preparations. The Wassermann reaction has been negative repeatedly.

DISCUSSION

DR. A. FLETCHER HALL JR., Santa Monica, Calif.: In view of the resistance to treatment in this case, I wonder if any one has tried the injection of starch, as is used in the treatment of lupus vulgaris.

DR. ARNE E. INGELS, San Francisco: The eruption has responded to roentgen therapy. I wonder how much of the present lesion is scarring due to applications of solid carbon dioxide and lactic acid.

Pyoderma Faciale; Acne Vulgaris. Presented by DR. ERVIN EPSTEIN, Oakland, Calif.

H. Y., a 38 year old white man, was presented before the San Francisco Dermatological Society on Feb. 14, 1942 (ARCH. DERMAT. & SYPH. **46**:314 [Aug.] 1942). Since then the patient has had six more typhoid-induced fever treatments, with some improvement. A test for bromides in the blood made after the patient had been constantly exposed to the bromide solution used in his employment as a photoengraver failed to reveal the presence of any.

DISCUSSION

DR. MAXIMILIAN E. OBERMAYER, Los Angeles: The clinical features of this interesting case suggest the influence of bromides. There is a possibility that the inflammatory process is kept active by constant absorption of bromides. I do not think that the negative reaction to the test for bromides eliminates this possibility. It can be ruled out only by a change in occupation.

DR. FREDERICK G. NOVY JR., Oakland, Calif.: I suggest that this patient has lupus erythematosus superimposed on old acne vulgaris. I think it is a mistake to use the term "pyoderma faciale" unless one is referring to the cases reported by O'Leary and Kierland (ARCH. DERMAT. & SYPH. **41**:451 [March] 1940) in which there were oval lesions containing a cystic purulent material. They characteristically start in the late teens or early twenties and subside in four to six months. They should not be confused with the scarring type of acne vulgaris.

DR. MERLIN T. R. MAYNARD, San Jose, Calif.: I originally raised the question of bromoderma in this patient. Despite the failure to demonstrate bromides in the blood, I believe that he should be given a therapeutic test of daily intravenous injections of sodium chloride.

DR. HARRY E. ALDERSON, San Francisco: White bread is another possible source of bromides. Although the amount contained is small, excessive eating

of bread might lead to a bromoderma. It would be interesting to try autoinoculation and to see the type of lesion developing from such a procedure.

DR. FRANK E. CORMIA (by invitation), Montreal, Canada: I wondered if any cultures had been made. In the cases reported by O'Leary and Kierland the results of bacteriologic studies were normal.

DR. ERVIN EPSTEIN, Oakland, Calif.: Dr. Maynard suggested the possibility of a bromoderma at the time of the previous presentation. This possibility cannot be denied. However, the patient had much more contact with the bromide solution during the week prior to the test than he normally did. Both cutaneous and respiratory contact was made. Despite this, an efficient laboratory failed to find any bromides in a specimen of blood. It seems likely that if enough bromides were being absorbed to produce a bromoderma, laboratory tests should reveal it. Both intravenous and oral sodium chloride will be given in an attempt to prove or disprove the diagnosis of bromoderma. The eruption is basically pustular, with secondary erythema and keloid formation. I doubt whether the diagnosis of lupus erythematosus is tenable for this reason. As I understand it, pyoderma faciale occurs in young adults or middle-aged patients. Scarring and keloid formation is said to be a characteristic feature of the disease. While no bacteriologic studies have been made, sulfathiazole, sulfanilamide and staphylococcus toxoid have not made any impression on the lesions.

Perlèche and Cheilitis. Presented by DR. NORMAN N. EPSTEIN, San Francisco.

G. R., a 53 year old white housewife, entered Mount Zion Hospital on April 15, 1942, complaining of dryness of the mouth, scaling of the lips and fissuring of the angles of the mouth of two days' duration. Two weeks prior to her entry an infection of the upper respiratory tract had developed. She had a similar episode in 1931, that subsided without treatment in six weeks. During the interval her lips seemed normal. She has been on a diet of approximately 1,000 calories per day, low in protein, calcium, iron, vitamin A, thiamine hydrochloride, nicotinic acid and ascorbic acid. Further study reveals that her diet has been deficient in the aforementioned vitamins since early childhood. During the course of her febrile episode she subsisted on little solid food, primarily starches.

Her lips show a crusting, exfoliating, yellowish lesion on the lower vermilion border. The mucosa of the vestibule of the mouth is moderately cyanotic but smooth. The upper lip shows slight changes similar to those on the lower lip. At the angles of the mouth, extending downward and outward, are multiple pinpoint-sized vesicles and small superficial fissures. The tongue shows normal papillae and substance without any tremor. There is slight cyanosis of the tongue.

The patient was given a vitamin-free diet on April 15, 1942. On April 18 she started with 10 mg. of riboflavin daily. By April 21 the lesions at the corners of the mouth had become less evident and the lesion on the lip accentuated. After she had been taking 300 mg. of nicotinic acid amide daily in addition to the riboflavin, the lesions at the corners of the mouth had cleared, but the lesion on the lip had failed to improve. On April 25 a high vitamin diet augmented by 10 mg. of thiamine hydrochloride was prescribed.

DISCUSSION

DR. C. JULIAN LUNSFORD, Oakland, Calif.: I have used large doses of riboflavin in a number of cases of cheilitis. However, in none of them did the disease respond well.

DR. ARNE E. INGELS, San Francisco: I should like to mention 2 interesting cases of cheilitis. One patient responded to local applications of a sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) ointment. The other, a woman, responded well to an estrogen applied in the form of an ointment. However, discontinuation of use of this ointment resulted in prompt recurrences. I doubt if the ointment base was responsible for the benefit obtained, as other ointments did not affect the condition favorably.

DR. NORMAN N. EPSTEIN, San Francisco: Riboflavin deficiency has been unusual in my experience. The eruption in this case differs from the ordinary cheilitis or perlèche by its dull cyanotic color. The therapeutic effect in this case was not dramatic.

DR. NELSON PAUL ANDERSON, Los Angeles: The most decided example of cheilitis that I have ever seen occurred in a patient presenting the Plummer-Vinson syndrome. I wonder if the deficient diet in this patient is due to a difficulty in swallowing.

DR. NORMAN N. EPSTEIN, San Francisco: The patient has been on a deficient diet for years because of an intestinal condition and hemorrhoids. She has been careful to eat a nonresidue diet of her own selection. However, this was not because of any inability to swallow.

A Case for Diagnosis (Ulcers on the Legs). Presented by DR. FRANK H. STIBBENS, Oakland, Calif.

B. F., a 29 year old Filipino, has had recurrent ulcers on his legs since 1935. The lesions are said to start as erythematous patches, which weep and break down to form ulcers. These heal in five to six months. The present attack started four months ago and followed an eczematous eruption on his ears, arms and legs. At present the patient has three ulcers involving both legs about halfway between the knee and the ankle. The lesions are sluggish but show some tendency toward healing. They measure from 1½ to 2½ inches (4 to 6.5 cm.) in diameter.

The Wassermann reaction was negative. An intradermal tuberculin test with a dilution of 1:1,000 elicited a strongly positive reaction. Mycelial threads have been found in pus taken from the ulcers on three occasions.

Potassium iodide by mouth, sulfanilamide locally and cod liver oil locally failed to affect the lesions.

DISCUSSION

DR. PAUL D. FOSTER, Los Angeles: The lesions suggested erythema induratum or a dermatitis factitia to me; they seemed very unusual.

DR. FRANCES TORREY, San Francisco: I suggest making a blood count. The possibility of sickle cell anemia suggests itself.

DR. KENDAL FROST, Los Angeles: I suggest the possibility of the lesion's being an artefact.

DR. A. FLETCHER HALL, Santa Monica, Calif.: These ulcers have a peculiar appearance suggesting a dermatitis factitia. They do not seem to be characteristic of any familiar entity. The attitude of the patient also suggests this diagnosis.

DR. ANKER K. JENSEN, Los Angeles: My first impression was neurotic excoriations and the second an infection with anaerobic streptococci.

DR. FRANK H. STIBBENS, Oakland, Calif.: The patient is anxious to enter the army, and he is distressed that these lesions may make it impossible. The interesting feature is that these ulcers are always preceded by an eczematous eruption. I have watched them develop, and they first appear as a little scratch which progressively enlarges. I have seen no evidence of self-inflicted injury.

Hypertrophic Lymphedema. Presented by DR. ARNE E. INGELS, San Francisco.

G. G. H., a 54 year old white man, was seen on Dec. 1, 1941 because of lymphedema of his left leg with secondary pyogenic infection.

The patient was given a cream containing 3 per cent sulfathiazole (2-[para-aminobenzenesulfonamido]-thiazole) and confined to bed for two months. During this time the involved leg lost all of its edematous papillomatous proliferating appearance.

Blood counts and urinalyses failed to reveal any findings of significance.

Epithelioma Adenoides Cysticum. Presented by DR. ARNE E. INGELS, San Francisco.

Mrs. A. S., a 34 year old white woman, had a number of lesions of her face twenty-one years ago. They have failed to change during the past twenty years. The patient is obviously hypertonic. She has been oppressed by family worries and fear of high places, steep streets, etc.

The patient presents an extensive eruption consisting of confluent shiny, reddish brown papules and nodules extending from the root of the nose to the sides of her nose, cheeks, nasolabial folds, upper lip and chin.

DISCUSSION OF CASE OF HYPERTROPHIC LYMPHEDEMA AND CASE OF EPITHELIAL ADENOIDES CYSTICUM

DR. ANKER K. JENSEN, Los Angeles: I merely wish to compliment the presenter on the fine therapeutic results obtained in both cases. However, I would not say that the sulfathiazole cream was the only therapeutic agent employed in the case of G. G. H.

DR. HIRAM E. MILLER, San Francisco: The patient was hospitalized for two months. This probably played a major role in the clearing of the edema.

DR. HARRY C. L. LINDSAY, Pasadena, Calif.: The method of local treatment with a sulfonamide compound is excellent. I used a sulfanilamide ointment on a resistant ulcer of the leg measuring 5 inches (13 cm.) across. This healed in one week (ARCH. DERMAT. & SYPH. **42**:357 [Aug.] 1940).

DR. ARNE E. INGELS, San Francisco: These cases were presented because of the response to therapy. The use of a sulfathiazole cream was effective in combating the secondary infection in the first case. In the second case solid carbon dioxide produced a decided improvement.

A Case for Diagnosis (Granuloma Annulare? Sarcoid?). Presented by DR. ARNE E. INGELS, San Francisco.

O. O., a 15 year old schoolboy, has had slowly enlarging lesions on his ears for the past year. He presents multiple pea-sized movable nodules in the aforementioned locations. These feel firm and measure 2 to 3 mm. in diameter.

Histologic examination of a specimen from one lesion shows a nonspecific granuloma of tuberculoid structure with many epithelial cells but no giant cells. Variously sized histiocytes and foam cells suggest rhinoscleroma. Gram stains have failed to show Bacillus capsulatus.

DISCUSSION

DR. NELSON PAUL ANDERSON, Los Angeles: I think this eruption is typical of granuloma annulare involving the ears. Incidentally, the patient has three pea-sized nodules on his left elbow, which appear as though they will eventually form a circle. The histologic picture is interesting. There are multiple areas of necrobiosis explaining the confusion between granuloma annulare and necrobiosis lipoidica diabeticorum. Some of the members will recall the demonstration of lipoidosis presented at the meeting of the American Academy of Dermatology and Syphilology in 1940. Some of the cases in which there were lesions on the backs of the hands were presented as instances of necrobiosis lipoidica diabeticorum. However, to me, the lesions suggested granuloma annulare clinically.

DR. MERLIN T. R. MAYNARD, San Jose, Calif.: I think these lesions are typical of granuloma annulare. Erythema elevatum diutinum might be considered in the differential diagnosis.

DR. STUART C. WAY, San Francisco: I agree that this patient has granuloma annulare, both clinically and histologically.

DR. ARNE E. INGELS: Histologically one would have to consider sarcoid, granuloma annulare, rhinoscleroma and leprosy. Clinically, the lesions were not annular, causing confusion in the diganosis.

Erythema Multiforme. Presented by DR. FREDERICK G. NOVY JR., Oakland, Calif.

F. R., a 68 year old white widow, was first seen in the University of California dermatologic clinic on April 8, 1942. Since 1932 she has had an eruption characterized by remissions and exacerbations. The eruption first appeared on the legs following an attack of influenza. Since then a generalized eruption has appeared about once a year and has persisted for about three weeks each time. The lesions on the legs are constantly present. In 1937 her mouth and throat were involved during a severe exacerbation. During the past year the attacks have been occurring every two to three months. Two weeks prior to her first visit here, she was given sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) for an acute inflammation of her external ears.

When first seen, she presented small papular erythematous lesions in annular and circinate patterns. They were most prominent on her trunk. In addition, there were tiny purpuric and pigmented scaling macules on her legs. She has chronic dermatophytosis and onychomycosis of her feet.

A general physical examination gave normal results. Roentgen examination of her paranasal sinuses and of her chest revealed no abnormalities. Dental roentgenograms demonstrated apical rarefaction of one tooth.

The urine was normal. A hemogram was also within normal limits. The platelet count was 330,000 per cubic millimeter.

DISCUSSION

DR. HARRY C. L. LINDSAY, Pasadena, Calif.: In some cases of erythema multiforme the condition imitates urticaria bullosa or pemphigus. The best treatment for erythema multiforme is the intravenous injection of 1/6 grain (0.01 Gm.) of mercuric cyanide. In most instances this will abort the eruption.

DR. FREDERIC G. NOVY JR., Oakland, Calif.: Such toxic eruptions are often seen. No definite focus of infection has been found despite the fact that the eruption has persisted for ten years. The patient has been examined on a number of occasions without the disclosure of such a focus. The eruption has been controlled in the past by the use of moccasin venom.

A Case for Diagnosis (Poikiloderma Vasculare Atrophicans?). Presented by DR. ROBERT A. STEWART, San Francisco.

E. B. L., a 54 year old woman, was presented before the San Francisco Dermatological Society on Dec. 3, 1937 (ARCH. DERMAT. & SYPH. **38**:140 [July] 1938) and before the American Dermatological Association, Inc., on June 8, 1938 (ibid. **39**:1054 [June] 1939).

DISCUSSION

DR. HIRAM D. NEWTON, San Diego, Calif.: I noticed an infiltration along the ulnar side of her left forearm. This was a slightly subcutaneous linear induration extending almost from the wrist to the elbow. In addition, she presented a similar infiltration on the right forearm. I am unable to explain the significance of this finding or to state whether it is associated with the peculiar cutaneous manifestations.

DR. MAXIMILIAN E. OBERMAYER, Los Angeles: While many of the features in this case suggest a diagnosis of poikiloderma vasculare atrophicans, certain changes made me consider the possibility of mal del pinto. Questioning this patient, who was born in Guatemala, revealed that she had the eruption commonly known as *empeines* at the age of 6 or 7 years. *Empeines* has been proved to be the early stage of mal del pinto. However, the natives of Mexico and of Guatemala use this term for a number of etiologically unrelated eruptions. Consequently, this woman's statement cannot be accepted as establishing the fact that she had early lesions of mal del pinto. What was the result of the Wassermann test?

DR. ROBERT A. STEWART, San Francisco: The question of mal del pinto has been considered. At the presentation before the American Dermatological Association, Inc., in 1938, Dr. Howard Fox discussed this phase of the subject. The Wassermann reaction was negative. The peculiar blue color seen in mal del pinto is not present. Dr. Fox felt that the disease in this case was not mal del pinto.

DR. MAXIMILIAN E. OBERMAYER, Los Angeles: The pigmentary changes are compatible with a diagnosis of late mal del pinto. The hyperpigmentation is replaced by depigmentation in this stage. The negative Wassermann reaction, however, eliminates the possibility of this diagnosis because the complement fixation and precipitation reactions are always strongly positive in the late stages of mal del pinto.

DR. HARRY C. L. LINDSAY, Pasadena, Calif.: I think the diagnosis of leprosy should be considered in this case.

A Case for Diagnosis (Generalized Erythematous Papular Eruption?).
Presented by DR. FRANK E. CORMIA (by invitation), Montreal, Canada.

Mrs. O. P., a 36 year old housewife, was first seen in the University of California dermatologic clinic in 1928. She presented a generalized pruritic excoriated erythematous scaly eruption on the face and shoulders. Her family physician stated that the patient's two sisters had had a similar eruption since childhood. The possibility of the eruption representing a tuberculid was considered, and the patient was given twelve intravenous injections of gold sodium thiosulfate.

She was not seen again until July 1937. Her eruption was unchanged. She complained of dyspnea and palpitation on exertion. An electrocardiogram showed a sinus tachycardia without evidence of myocardial damage. In September 1937 she returned complaining of fever, malaise and fatigability. The physical examination revealed only normal findings. Roentgen examination of the chest was normal. The results of agglutination tests were negative for typhoid, paratyphoid A, paratyphoid B, Bacillus enteritidis and undulant fever. A hemogram was essentially normal. The basal metabolic rate was +9 per cent.

Histologic examination of a specimen of skin showed only a chronic inflammatory reaction.

DISCUSSION

DR. KENDAL FROST, Los Angeles: I suggest the diagnosis of atopic dermatitis and neurotic excoriations.

DR. HARRY E. ALDERSON, San Francisco: I believe the patient presents neurotic excoriations.

DR. NELSON PAUL ANDERSON, Los Angeles: I agree that the patient has neurotic excoriations on her arms and an atopic dermatitis on her face. There is a peculiar dermatitis involving the face in women with this same picture. There always seems to be wrinkling on the upper lip and around the mouth. Several patients with this dermatitis that I have seen appeared to have had too much roentgen therapy. The condition is an atopic dermatitis, but I believe that it is a special form.

DR. HARRY C. L. LINDSAY, Pasadena, Calif.: The patient may have an atopic dermatitis, but I think she also has lupus erythematosus.

DR. FRANK E. CORMIA (by invitation), Montreal, Canada: When I first examined this patient, I thought she had lupus erythematosus. However, she has had these lesions on her face for fifteen to twenty years with little or no atrophy. She has not received any roentgen therapy. She also presents neurotic excoriations. The excoriated lesions are more pronounced on the left arm than on the right, and she is right handed. On the other hand, the lesions on the face could not be included in this category. I have not seen atopic dermatitis on the face with this clinical appearance. Histologically, the lesions on the face suggested lupus erythematosus. The lesions on the body are characterized by burning. This

is not characteristic of atopic dermatitis. There is some tendency toward grouping of the lesions. There is considerable residual pigmentation with some atrophy.

DR. MERLIN T. R. MAYNARD, San Jose, Calif.: The lesions on her back are identical in appearance with those on her arms except that they are not excoriated. The patient may scratch a lesion on her arm after it appears, but I do not believe that the excoriations are primary lesions.

Pemphigus Vulgaris. Presented by DR. NORMAN N. EPSTEIN, San Francisco.

I. S., a 44 year old white woman, first had bullae on the sides of her nose in March 1941. During the next few months similar lesions developed on her scalp, chest, back and limbs and in her mouth. While the eruption has varied in intensity, she has never been free of lesions since the onset. The lesions consist of fragile bullae which rupture in three to five days after making their appearance and undergo involution completely in about ten days. New bullae are interspersed with old lesions. There is little inflammatory reaction about them.

A general physical examination revealed normal findings. The urine was normal. The Wassermann and Kahn reactions were negative. The nonprotein nitrogen content of the blood was 27.1 mg. per hundred cubic centimeters. A blood count showed a mild secondary anemia.

Therapy has consisted of dihydrotachysterol in doses of 25 to 50 mg., vitamin D in doses of 150,000 to 400,000 U. S. P. units a day and solution of potassium arsenite U. S. P. Limited improvement occurred with the use of vitamin D.

DISCUSSION

DR. HARRY C. L. LINDSAY, Pasadena, Calif.: Dr. Samuel Ayres obtained benefit in some patients with pemphigus by the use of sulfanilamide. An extract of adrenal cortex (2 to 5 cc twice a day) has been used in some cases of pemphigus with benefit. Pemphigus confined to the mouth and lips is frequently less malignant than the generalized form. Such patients may live seven or eight years or longer, although the ultimate termination is to be expected in such cases.

DR. ARNE E. INGELS, San Francisco: It would appear logical to use sulfonamide drugs locally.

DR. NORMAN N. EPSTEIN, San Francisco: This is an unusually benign type of pemphigus. Dihydrotachysterol seemed to be of some benefit, but its effect has not been dramatic in this or other cases in which I have used it.

DR. ERNEST K. STRATTON, San Francisco: I have been looking for a case of pemphigus to test the therapeutic effect of rabies vaccine. Experimental work has shown that the virus of pemphigus cannot be inoculated into animals infected with rabies. The converse also holds true: Animals infected with pemphigus cannot be inoculated with rabies virus. This suggests a therapeutic approach in such cases.

A Case for Diagnosis (Vascular Tumor?). Presented by DR. ARNE E. INGELS, San Francisco.

F. V., a 33 year old white housewife, has had a slowly enlarging, asymptomatic eruption on her face for the past twenty years. The left side is involved much more than the right. The patient presents multiple tumor formations almost at the level of the skin associated with extensive telangiectasia.

DISCUSSION

DR. PAUL D. FOSTER, Los Angeles: I am unable to make a definite diagnosis, but I suggest an angiolupoid or merely telangiectasia.

DR. MERLIN T. R. MAYNARD, San Jose, Calif.: I should consider the condition in this case an extreme example of ectasia.

DR. FRANK H. STIBBENS, Oakland, Calif.: I should classify this eruption as a nevus.

A Case for Diagnosis (Lymphoblastoma?). Presented by DR. NORMAN N. EPSTEIN, San Francisco.

M. F., a 69 year old white woman, has had a generalized erythematous eruption for the past few years. About six months ago multiple plaques and tumors appeared on various parts of her scalp, body and extremities.

A general physical examination revealed only normal findings. A hemogram was also normal.

A biopsy revealed a bandlike infiltrate involving the entire corium extending into the subcutaneous tissue.

DISCUSSION

DR. PAUL D. FOSTER, Los Angeles: I considered this eruption to be a reasonably typical example of mycosis fungoides.

DR. HARRY E. ALDERSON, San Francisco: I agree with the diagnosis of mycosis fungoides.

DR. C. JULIAN LUNSFORD, Oakland, Calif.: I have given a patient with mycosis fungoides intravenous injections of radioactive phosphorus. It is too early to evaluate the results.

DR. HIRAM E. MILLER, San Francisco: I treated a patient with mycosis fungoides with radioactive phosphorus without benefit. It was unfortunate that the man had received large doses of roentgen therapy previously and the lesions were no longer radiosensitive. It seems doubtful whether it is wise to use radioactive phosphorus, which is deposited in the bones, when the lesions are on the skin. Radioactive arsenic, which is deposited in the skin, would be a better preparation if it were available.

DR. C. JULIAN LUNSFORD, Oakland, Calif.: Dr. Lawrence stated that he performs a biopsy of material from the lesion and from the normal skin five days after the injection. The amount of radioactive substance in each is determined, and from this he feels that the indication for further treatment can be judged.

DR. ERVIN EPSTEIN, Oakland, Calif.: I treated a patient with hemorrhagic sarcoma of Kaposi with radioactive strontium. This did not affect the lesions, which later responded to roentgen treatments. The patient received sufficient radiation to produce a severe anemia. Biopsy studies proved that little or no radiation entered the skin after the intravenous injection of the aforementioned preparation. Seven patients with psoriasis were treated with small doses of the same preparation with good results in only 2 instances. Radioactive sulfur, which apparently can be produced in small amounts, is deposited in the skin and seems the logical choice.

DR. HARRY C. L. LINDSAY, Pasadena, Calif.: Mycosis fungoides is considered to be a cutaneous disease, but extension to the internal organs often occurs. I had a patient who responded temporarily to bismuth and sodium tartrate and later to gold sodium thiosulfate. She received twenty-one doses of the last-mentioned preparation in amounts ranging up to 100 mg. Postmortem studies failed to reveal any evidence of damage from the gold sodium thiosulfate.

DR. ALBERT C. SHUMATE, San Francisco: It is interesting that this patient has been seen in every dermatologic clinic in San Francisco as well as in clinics in other parts of the country. In most instances the eruption was diagnosed as an allergic dermatitis.

DR. NORMAN N. EPSTEIN, San Francisco: I had the opportunity of observing this patient while the eruption changed from an eczematoid dermatitis to an actual lymphoblastoma. I should prefer to consider the eruption as a lymphoblastoma rather than as mycosis fungoides, because of the histologic picture.

Book Reviews

The Biology of the Negro. By Julian Herman Lewis, Ph.D., M.D., Associate Professor of Pathology, University of Chicago. Price, $5.00. Pp. 407. Chicago: The University of Chicago Press, 1942.

For the first time, an author has assembled in a book facts which have been observed and reported concerning the biology (including pathology) of the Negro. This book is essentially a study of comparative anatomy and pathology of the Negro and of the Caucasian race. The author states that he has no thesis to develop or disprove. He has chosen what he considers the most important data contained in a voluminous literature. Some articles have been disregarded as inconsequential and others as obviously biased and written for purposes of propaganda. The material contained in the book includes data on both African and American Negroes.

The first chapter deals briefly with population and vital statistics. The second chapter describes at considerable length the anatomy of the Negro, including pigment of the skin, mucous membranes and nails, sweat glands, configuration of the palms and soles and various types of hair. This is followed by a short chapter on biochemical and physiologic characteristics, including the function of the Negro skin in resisting actinic rays and heat, specific racial odors and the response of the Negro to drugs.

The remaining part of the book, occupying three fourths of its contents, deals with various diseases affecting the Negro, comparing their morbidity and mortality with these factors in the white race.

A chapter devoted to diseases of the skin contains 24 pages, and one on syphilis has 28 pages. Many other diseases are discussed in the chapters on medical and surgical diseases, including cancer, keloid, yaws, leprosy, the exanthems, lymphogranuloma venereum, pellagra, von Recklinghausen's disease and mongolian spots. Considerable space is devoted to sickle cell anemia, which is almost entirely confined to the Negro race and which is of interest to dermatologists on account of the ulcers of the legs, which occur in 40 per cent of cases.

Among the diseases which are extremely rare in the skin of the Negro are cancer and precancerous conditions, such as senile keratoses, xeroderma pigmentosum and sailor's skin. Diseases which are rare or uncommon include psoriasis, leukoplakia and pediculosis.

Diseases which are especially common in the Negro include keloid and elephantiasis (so called fibroid diathesis), granuloma inguinale, dermatosis papulosa nigra and ainhum.

A unique characteristic of the Negro skin, the author states, is its resistance to external irritants. This was exemplified during World War I, when Negroes were employed in the manufacture of certain explosives. The Negro also suffers less often than the white man from poison ivy dermatitis, from ill effects of ultraviolet rays and from miliaria.

Although the subject of tuberculosis in general is fully discussed, little is said about its cutaneous manifestations. No mention is made of some of the finer distinctions in tuberculosis of the skin observed in the United States in recent years.

Racial differences in syphilis include the greater frequency of the disease and greater liability to cardiovascular changes in the Negro than in the white race. The reasons for the latter are not clear according to the author. Racial differences in involvement of the central nervous system are thought to be questionable. Mention is made of the special tendency of the Negro to suffer from the annular papular syphilid.

Conclusions can be drawn that the liabilities of the Negro are chiefly his morbidity and mortality from heart disease, tuberculosis and syphilis. His assets are his birth rate, physical stamina, excellent teeth and resistance to malaria, yellow fever and the exanthems. The balance is in favor of the Negro.

The volume should be of interest to anthropologists, sociologists and physicians. It should be an invaluable book of reference for the dermatologist. In spite of its containing many statistical data, with nearly 1,350 bibliographic references, it is a readable and unusually well written book.

The work of the publisher is entirely satisfactory.

Manual of Dermatology. Issued under the auspices of the Committee of Medicine of the Division of Medical Sciences of the National Research Council. By Donald M. Pillsbury, M.D., Marion B. Sulzberger, M.D., and Clarence S. Livingood, M.D. Price, $2.00. Pp. 421, with 109 illustrations. Philadelphia: W. B. Saunders Company, 1942.

This manual of dermatology is one of a series of volumes written under the auspices of the Division of Medical Sciences of the National Research Council to provide the medical departments of the United States Army and Navy with concise, essential information for use in the field of military medicine. Since diseases of the skin and venereal infections accompanied by cutaneous manifestations comprise 20 per cent of all diseases in the armed forces and are of greater importance in military than in civil life, this compact manual fills an urgent need.

In chapter 3, entitled Diagnosis Based on Distribution, most of the illustrations are good, but figure 7 is confusing, because six common forms of drug eruptions are represented in one figure. Figure 10, illustrating the sites of herpes zoster, is also misleading, because the several neural distributions are all represented in one figure. Chapter 4, dealing with the diagnosis of eruptions of commonly involved sites, is excellent and should be especially helpful to the medical officer who is not a dermatosyphilologist. The accompanying full page photographs are fairly good. On page 115, in figure 78, a mistake was overlooked when the cause of granuloma inguinale was given as Leishman-Donovan bodies instead of Donovan bodies.

Chapter 5, on the principles of local treatment, is presented in a practical manner. It includes the standard useful procedures and the modern advances in dermatologic therapy. Treatment is divided into two types: (1) simplified treatment for the isolated station or small ship and (2) the hospital or sick bay extended treatment. The recommended formulary found in the appendix is also divided into a simplified formularly for the smallest unit of the medical corps and the hospital formulary for the general and large station hospitals. Pages 158 to 161, on roentgen treatment, might well have been omitted, because the book was written principally for the medical officer who is not a dermatologist.

The separate chapters on fungous infections, pyodermas, parasitic infestations, plant dermatitis and penile lesions are among the most important. The diagnosis and treatment of these cutaneous diseases are clearly and concisely presented.

Emphasis has been placed on the common diseases of the skin affecting persons in the age-sex group found in the Army and Navy. Diagnostic and laboratory procedures include only those which are simple and useful. The authors live up to their objective in setting forth briefly and simply the management of cutaneous diseases of high incidence in the armed forces.

The manual is small, measuring 8 by 5½ inches (20 by 14 cm.). The format is excellent, and the index is ample, covering 36 pages.

Physician's Reference Book of Emergency Medical Service. Pp. 268. New York: E. R. Squibb & Sons, 1942.

This book has been printed and distributed as a public service to physicians in the Emergency Medical Service of the United States of America by the medical department of E. R. Squibb & Sons. Compiled mainly from British medical literature and in part from American sources, it presents practical experience

acquired in handling civilian war casualties. The articles are taken from the *Military Surgeon,* from the *Lancet,* from bulletins of the Office of Civilian Defense, in Washington, D. C., and from British government printing offices.

The book is divided into three sections: Section 1 deals with precautionary measures for the protection of hospitals and civilian health. Section 2 deals with the organization of hospital services in relation to first aid and reception of casualties. Section 3 deals with the management of casualties and contains articles on shock, burns, wounds and fractures, blast injuries, crush injuries and war gas injuries.

Much space is given to the treatment of burns, and probably everything available in the literature with regard to this topic is mentioned. Much space is also given to gas injuries. The properties and effects of the different gases are presented in tables.

This reference book should be of value to every physician who is active in civilian defense or who wants to prepare himself for civilian emergencies.

Electrophoresis of Proteins and the Chemistry of Cell Surfaces. By Harold A. Abramson, Laurence S. Moyer and Manuel H. Gorin. Price, $6.00. Pp. 328. New York: Reinhold Publishing Corporation, 1942.

The movement of ionized particles under the influence of an electric current is electrophoresis. This book by Abramson and his collaborators deals with the phenomenon in a fundamental way. The book is primarily for the biologist well grounded in electrophysics. However, the subject matter is of special interest to the dermatologist, since the skin is a semipermeable membrane on which these phenomena may be studied and observed.

Furthermore, cataphoresis may be used as a method for introducing therapeutic agents into the skin and through it to the general circulation; in fact, this method is already in use. The book devotes some pages to the skin, and comment is made on the application of electrophoresis in therapy and for the dermatologist.

The book is recommended for the dermatologist, even though the electrophysics may be beyond him. In therapy and clinical investigation, physicians are frequently called on to use modalities conceived and elaborated in an allied science. An understanding of the principles and concepts of this science must at some time and in some way be approached by the practitioner who would seek to have more than a superficial understanding of the instruments he uses.